The role of familial factors in the associations between sickness absence and disability pension or mortality

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Background: Little is known about the factors influencing the future situation of individuals on sickness absence (SA) or disability pension (DP). The aim was to investigate whether being sickness absent is associated with future DP and premature death, and whether such associations can be explained by familial factors. Methods: A sample of 45 734 Swedish twins was followed for 13 years. Cox proportional hazard models were applied to analyse the associations between having a new SA spell/being granted DP in 1995 and DP/mortality during follow-up 1996–2008. The familial confounding was tested by studying twins that were different in their exposure to SA and DP, respectively, during 1995. Results: SA strongly predicted DP during a follow-up of 13 years, in both women [hazard ratios (HR) 3.03, 95% confidence intervals (CI) 2.82–3.25] and men (HR 3.83, 95% CI 3.50–4.18). A minor part of the associations seemed to be explained by familial factors. Both SA and DP increased risk for mortality. For SA, HR was 1.46 (1.27–1.69) for women and 1.31 (1.14–1.51) for men. For DP, HR was 1.38 (0.92–2.05) for women and 1.73 (1.24–2.42) for men; results suggested a small influence of familial factors. Conclusion: SA was found to be a long-term risk factor for DP and premature death, in both women and men. Familial factors played no or a minor role for these associations. Being granted DP in 1995 also increased risk for premature death, with a slight indication of familial influences in both sexes.

Introduction

Work incapacity in terms of sickness absence (SA) or disability pension (DP) is considered a major public health problem with possible severe consequences for individuals, employers and society. At an individual level, being on SA or DP may have negative implications for future health, life style, economy, career development, social integration or mortality. The research on the consequences of SA and DP is scarce; so far most of the existing studies have focused on risk factors for SA. A few previous studies have reported that SA predicts future DP and mortality, as well as that DP predicts premature death. However, little is known about how these associations develop, that is, what factors, in addition to those related to the underlying disorder, may influence the consequences of being on SA. To the best of our knowledge, no studies have examined whether associations between SA and future DP or mortality could be explained by familial factors. Twin studies provide us with a unique possibility to investigate the influence of familial factors on the consequences of SA and DP. Familial factors are the factors that contribute to the similarity of twins in a pair. Depending on the zygosity, twins in a pair may share either 100% (monozygotic, MZ) or on average 50% (dizygotic, DZ) of their common genetic make-up. In addition to a similarity depending on the common genes, twins may also become more alike owing to the environment they experience together, i.e. shared (mainly childhood) environment. One way to control for familial factors is to follow the development of the consequences in twin pairs that are discordant or differently exposed to SA or DP at the start of follow-up. Analyses of twins that are identical for the familial factors but different for their predictor in terms of SA or DP can help us to understand the underlying pathways in the associations. The influence of familial factors will be indicated if associations seen in the whole cohort of twins will substantially change or disappear in discordant twin pair analyses. In contrast, similar associations in discordant twin analyses, as compared with the whole cohort, will suggest that factors specific to each individual (e.g., choice of education or workplace, or experienced injuries) are more important for the studied associations.

Two recent prospective studies of twins showed that liability to DP owing to different diagnoses was moderately explained by genetic factors, irrespective of the age when the DP was granted. Genetic factors were demonstrated to differ between women and men. That is, different sets of genes in women and men seemed to be involved in liability to DP. The remaining variation in liability to DP was explained by environmental effects specific to each individual. Findings presented in these studies suggest that familial factors may also contribute to the associations between SA and its consequences and potentially act differently among women and men. The aim of this study was to (i) examine SA as a risk factor for DP and mortality in a Swedish twin cohort of women and men followed for 13 years, as well as (ii) to study if familial factors may be of importance for these associations.

Methods

Participants and data sources

Data from a population-based prospective Swedish twin cohort STODS (Swedish Twin cohort Of Disability pension and Sickness absence) were used. STODS is a sub-sample of the Swedish Twin Registry (STR) and includes all twins that were born in Sweden between 1925 and 1958 (n = 59 598 individuals). Approximately one-third of all twins are MZ, one-third is same-sexed DZ, and one-third is opposite-sexed (OS) DZ twins. The zygosity was assigned by using questions about the twin intra-pair similarity in childhood. This method was also validated by DNA testing and had ≥99% accuracy.
The study sample included all individuals that were alive and living in Sweden on 1 January 1995 and still alive on 31 December 1995. Also, all individuals had to be at risk of SA or DP on 1 January 1995, that is, <65 years of age, not emigrated, not on old-age pension, nor on SA or DP, respectively. Twin pairs with unknown zygosity or with information available for only one co-twin (i.e., information on SA, DP, death, emigration or old-age pension was missing for one of the twins) were excluded from the data analyses. The final study sample included 45734 twin individuals, whereas 2401 male MZ, 3851 male DZ, 2779 female MZ and 4012 female DZ twin pairs, and 8410 OS twin pairs. The mean age at the baseline was 49.6 ± 7.6 years for women and 49.2 ± 7.5 years for men.

Data on zygosity and sex were obtained from STR. Data on sickness benefits and DP owing to any diagnosis (date of beginning and end, and duration of the first SA spell as well as starting date of DP) paid by the Social Insurance Agency were collected from the MiDAS-database from the National Social Insurance Agency. Information on education, employment status, year of emigration and old-age retirement was obtained from Statistics Sweden. Data regarding date of death were obtained from the National Board of Health and Welfare. Finally, all registry data were linked to the twin data by using the unique 10-digit personal identification number assigned to all Swedish residents.

All people living in Sweden are covered by the Social Insurance that provides sickness benefits when disease or injury has led to work incapacity, covering ~80% of lost income. DP can be granted when that work incapacity is permanent and, like old-age pension at the age of 65 years, covers ~65% of lost income. For employees, the first 14 days of an SA spell are generally paid by the employer. For those, information on the SA spells ≤14 days was not available through the MiDAS database.

Predictor variables
For the analyses of the associations between SA and DP or mortality, the predictor variable/exposure was the first new SA spell during the year 1995. That is, if an individual had several new SA spells during 1995, only information about the first new SA spell was included in the analyses. SA spells that had started before 1 January 1995 and continued into 1995 were not included. Each SA spell was followed until it ended, even if that was after 1995. Participants that had a new SA spell and also were granted DP during 1995 were excluded from the analyses. In the analyses, possible risk associated with (i) having a new SA spell in 1995, or not, and (ii) duration of a new SA spell, was assessed. Duration of the SA spell was categorized as 0, ≤30, 31–90, 91–180 or >181 days with sickness benefits from the Social Insurance Agency.

For the analyses of the association between being on DP and mortality, the predictor variable was defined as during 1995 being granted DP (yes/no) for the first time. All DP cases owing to any medical diagnosis that started after 1 January 1995 were included into analyses.

Outcome variables
All participants were followed from 1 January 1996 to 31 December 2008. For the analyses using SA spell as predictor, outcome variables included being granted DP and mortality during the 13-year follow-up until 2008. For the analyses using DP as predictor, the outcome variable was mortality during the follow-up until 2008.

Statistical analyses
Cox proportional hazard models were applied to estimate hazard ratios (HR) with 95% confidence intervals (CI) for being granted DP after having a new SA spell in 1995 as well as for mortality after having a new SA/DP in 1995. All analyses were adjusted for age and zygosity. Because the sample included twin pairs rather than independent individuals, the analyses were clustered on twin pair identity. The reference group included individuals that were not on SA or DP during year 1995. All analyses were also stratified by sex, and the significance of sex differences was tested by adding an interaction term to the Cox model, simultaneously containing the main variable of SA/DP in 1995.

Potential familial confounding was controlled for by analysing twin pairs that were discordant for a new SA spell or DP in 1995. That is, a twin pair was treated as discordant if one twin in a pair had a new SA or DP in 1995, whereas the twin partner did not. In discordant twin (i.e. co-twin control) analyses, twins in a pair are optimally matched on genetic and common environmental factors as well as for their sex and age at the baseline. Conditional Cox proportional models are applied and the sample is stratified by twin pair, providing each twin pair with their own baseline hazard. Influence of familial factors (genetic and common environment) will be indicated if the association found in the analyses of the whole cohort will disappear or change considerably in the analyses of discordant twin pairs. On the other hand, environmental factors not related to family background may be more pronounced if the association is seen in the analyses of both the whole sample and discordant twin pairs. Familial factors will be assumed to play a minor role if the association is found in the analyses of both the whole sample and discordant twin pairs. Ideally, discordant twin pair analyses could be performed for each zygosity group. However, in the present study, the number of discordant twins was low for studying SA of different duration and therefore the analyses were pooled on zygosity.

All statistical analyses were performed with SAS 9.2.20
The study was approved by the Stockholm Regional Ethical Review Board in Sweden.

Results
The cumulative incidences of an SA spell or being granted DP during year 1995 are presented in table 1. There were approximately equal proportions of women and men in the sample (50.8 and 49.2%, respectively). Thirteen percent of the women and 10% of the men had a new SA spell in 1995. Among those with a new SA spell in 1995, 5.9% of the women and 4.8% of the men had an SA spell of ≤30 days. Very few (1.2% of women and 0.8% of men) had a new SA spell that lasted between 91 and 180 days. Approximately 1.15% of the women and 0.88% of the men were granted DP in 1995. During the follow-up years 1996–2008, ~16% of the women and 12% of the men were granted DP. Moreover, 5.6 and 8.1% of women and men, respectively, died during the follow-up.

Association between sickness absence and disability pension
Having a new SA spell in 1995 strongly predicted the risk of DP during the follow-up as compared with not having a new SA spell in 1995, in both women (HR 3.03, 95% CI 2.82–3.25) and men (HR 3.83, 95% CI 3.50–4.18; table 2). The difference in HR for women and men was statistically significant (PInteraction < 0.001) (data not shown). After controlling for familial confounding, the HR for DP remained significant in both women (HR 2.45, 95% CI 2.07–2.91) and men (HR 3.34, 95% CI 2.66–4.34) (table 2). Again, the sex difference in HR was significant (PInteraction = 0.04).

A longer duration of the first new SA spell in 1995 implied gradually increasing HRs for DP during the following 13 years, in both women and men. HRs were consistently higher among the men compared with the women but the differences were only significant for SA spells of 31–90 and of 181–365 days (PInteraction(31–90) = 0.01, PInteraction(181–365) = 0.01). Familial factors seemed to have a small effect on almost all associations. An exception was for SA spell of 91–180 days among men. After controlling for familial background, the HR for DP after having an SA spell of 91–180 days dropped from
HR 4.41 to 2.56 (95% CI 1.18–5.52). Sex differences remained significant for the SA spells of 31–90 and of 181–365 days ($P_{Interaction}$ (31–90) = 0.03, $P_{Interaction}$ (181–365) = 0.01).

Associations between sickness absence or disability pension and mortality

Having a new SA spell in 1995 was a significant predictor of premature death during the follow-up compared with not having a new SA spell that year (for women HR 1.46, 95% CI 1.27–1.69 and for men HR 1.31, 95% CI 1.14–1.51; table 3). The HRs were higher among women than among men but the sex differences were not statistically significant ($P_{Interaction}$ = 0.26).

Analysis of twin pairs discordant for having a new SA spell in 1995 did not suggest any influence of familial effects on conditional HR.

The duration of the new SA spell in 1995 had impact; having an SA spell >90 days significantly increased the risk for mortality during the follow-up, in both women and men. The differences in HRs between women and men were not significant ($P > 0.10$). After taking familial confounding into account, the HRs changed slightly in both women and men (table 3).

Being granted DP during 1995 significantly increased the risk for mortality during the follow-up in men (HR 1.73, 95% CI 1.24–2.42) (table 3). The association was not statistically significant in women (HR 1.38, 95% CI 0.92–2.05). The difference between the sexes was not significant ($P_{Interaction}$ = 0.32). After controlling for familial confounding, the estimated risk for mortality dropped for men (HR 1.08, 95% CI 0.51–2.29).

Discussion

In the present study, we investigated the associations between SA and future DP and mortality, and whether familial (i.e. genetic and common environmental) factors were contributing to these associations. Having a new SA spell in 1995 was found to be a strong predictor of being granted DP during a follow-up of 13 years, with what appeared to be a small though consistent contribution by familial factors, in both women and men. Incidence of SA or DP in 1995 also increased the risk for mortality. Familial factors seemed to be less influential for these associations.

Our findings that being on SA increases the risk for future DP and premature death are consistent with the results from the few previous studies in this area.3,4,10,21,22 In contrast to previous research, we could shed more light on the mechanisms involved in these associations by following a large population-based sample of twins with a follow-up of 13 years. Specifically, the results revealed that familial factors only have a minor role in the association between SA and future DP, in both women and men. This suggests that having an SA spell tends to directly increase the risk for future DP rather than depend on the factors based on twin similarity, such as inherited traits or common (environmental) experiences (e.g. socioeconomic status in family). Small influences of familial factors hence indicate that the association may be influenced by other factors, such as socioeconomic status and work environment.

Table 1 Cumulative incidences (%) of number of twins having a new SA spell or granted disability pension (DP) during year 1995, and of being granted DP, or mortality during follow-up in 1996–2008

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Number of individuals (%) (n = 45 734)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women (n = 23 211)</td>
</tr>
<tr>
<td></td>
<td>All twins</td>
</tr>
<tr>
<td>Individuals having a new SA spell during 1995</td>
<td>3106 (13.38%)</td>
</tr>
<tr>
<td>Duration of the SA spell</td>
<td>20 105 (86.62%)</td>
</tr>
<tr>
<td>0 days</td>
<td>20 105 (86.62%)</td>
</tr>
<tr>
<td>≤30 days</td>
<td>1379 (5.94%)</td>
</tr>
<tr>
<td>31–90 days</td>
<td>1114 (4.80%)</td>
</tr>
<tr>
<td>91–180 days</td>
<td>277 (1.19%)</td>
</tr>
<tr>
<td>181–365 days</td>
<td>336 (1.44%)</td>
</tr>
</tbody>
</table>

Only twin pairs with information on both twins in a pair were included in the analyses.

Table 2 Cox proportional HR with 95% CI for the association between having at least one new SA spell in 1995 and being granted DP during follow-up 1996–2008 in a cohort of 45 734 twins (50.8% women)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Number of discordant twin pairs*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All twins</td>
</tr>
<tr>
<td></td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>A new SA spell in 1995 (reference group: no new SA spell in 1995)</td>
<td>3.03 (2.82–3.25)</td>
</tr>
<tr>
<td>Duration of the SA spell</td>
<td>1506</td>
</tr>
<tr>
<td>0 days</td>
<td>2.40 (2.16–2.66)</td>
</tr>
<tr>
<td>≤30 days</td>
<td>2.59 (2.32–2.89)</td>
</tr>
<tr>
<td>31–90 days</td>
<td>3.94 (3.25–4.78)</td>
</tr>
<tr>
<td>91–180 days</td>
<td>9.32 (7.76–11.20)</td>
</tr>
<tr>
<td>181–365 days</td>
<td>9.32 (7.76–11.20)</td>
</tr>
</tbody>
</table>

HR 4.41 to 2.56 (95% CI 1.18–5.52). Sex differences remained significant for the SA spells of 31–90 and of 181–365 days ($P_{Interaction}$ (31–90) = 0.03, $P_{Interaction}$ (181–365) = 0.01).
by environmental events that were not shared by twins, including choices of different education and occupation, or exposure to different environments or accidents. Previous studies have shown that factors that increase risk for future DP include, for example, lifestyle, marital status and living and working conditions, although familial factors seem to play a role in some of these associations.\textsuperscript{23–25} Future studies should focus on identifying these factors for better understanding of how SA predicts higher risk for DP also in a long-term perspective.

A finding that warrants attention is that the risk for future DP remained high irrespective of how short or long the initial SA spell was. That is, the results suggest that even short SA spells tend to increase risk for future DP. Clearly, all DPs are preceded by SA but only a few of those that are sickness absent are later granted DP. Also, SA is a common recommendation or ‘prescription’ in medical care and possible negative consequences are seldom discussed with the patient.\textsuperscript{26} This suggests that further research is needed to investigate the consequences, positive and negative, of being on SA, for different durations and owing to different medical diagnoses.\textsuperscript{1,2,27} Again, as the familial factors seemed to be of less importance for the association between having an SA spell and future DP, it is also crucial to identify contributions of environmental influences, including specific work environmental or psychosocial factors.

In contrast to our findings of SA as a risk factor for DP, short SA spells did not imply a significantly increased risk for mortality. Only SA spells that for >90 days were significantly associated with mortality, in both women and men. The results are in line with a previous study, where long-term SA significantly predicted mortality.\textsuperscript{5} After controlling for familial background, the estimates changed marginally, which suggest that familial factors were of less importance for this association.

Depending on type of the studied outcome following SA, different patterns of risk were observed among women and men. The risk for DP after a new SA spell in 1995 was consistently higher among men than among women. In contrast, the risk of premature death tended to be higher among women compared with among men, among those who in 1995 had a new SA or DP. This suggests that pathways for DP and mortality, respectively, might differ between women and men. More research is warranted to identify the factors explaining the sex differences in these associations.

DP was shown to significantly increase the risk for premature death in men, which is consistent with the findings of the few previous studies.\textsuperscript{8–10} The present study could further demonstrate that familial factors only contributed to the association to a small extent. Although the association lacked significance among women, worth noting is that after controlling for familial confounding, risk estimates changed into the opposite direction in women compared with that in men. This may suggest that different familial (genetic or environmental) factors may influence the association between DP and premature death, or that familial factors may have different roles for women and men.

Previous results from genetically informative studies of different disorders and DP suggest a moderate influence of genetic factors and negligible effects of shared environment.\textsuperscript{15,28,29} Thus, our findings that familial factors contribute to the association between SA/DP and mortality are likely to primarily reflect the genetic similarity between the twins in a pair. In addition to the genetic susceptibility to the disorder behind the SA/DP, the genetic factors may also reflect the susceptibility to other disorders (e.g. hypertension), functional capacity or chronic childhood disease; those conditions were shown to be partly heritable in previous studies.\textsuperscript{30–32}

The study has several strengths. The sample was large, population-based and was followed for as long as 13 years. Because all data were obtained by linking a number of national registers, there were no information or response biases. Information on all individuals was detailed and of high quality, with no loss to follow-up. However, several limitations should be kept in mind. First, owing to the small number of discordant twin pairs, separate analyses for MZ and DZ twins could not be performed. Thus, we had only the possibility to examine the influence of familial factors in general, and could not separate between genetic and shared environmental effects. In conjunct with this, the difference in HRs for the whole sample and for discordant twin pairs could not be formally tested. However, the theoretical background for discordant twin pair analyses is solid (see\textsuperscript{18,19}), providing strong control for familial confounding. Second, for employees, information on the first 14 days of an SA spell was not included. Thus, the associations between short SA spells and DP and mortality could not be studied. Also, as data on SA diagnoses were not available, we could not perform any diagnosis-specific analyses. Forth, as the data were not available, the analyses could not be adjusted for additional factors that have earlier been shown to influence DP (e.g. lifestyle or smoking).

In conclusion, the present study has demonstrated that SA, irrespective of duration, constitutes a long-term risk for future DP, in both women and men. Familial factors had a minor role for this association, suggesting that the association between SA and DP is owing to factors not shared by twins in a pair. Incidence of SA or DP also increased the risk for mortality with a slight indication of familial influences among women and men.
**Funding**

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**Conflicts of interest:** None declared.

**Key points**

- By using a large twin cohort, the present study replicates previous findings of sickness absence as a predictor of future disability pension and mortality.
- Factors making family members similar (i.e. genetic make-up and common environmental experiences) explain a small part of the associations between sickness absence and disability pension/mortality.
- The results suggest that factors influencing the association between being on sickness absence and disability pension or mortality are primarily environmental and, therefore, might be possible to modify.

**References**