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Article

A Life Course Study of Genetic and Environmental Influences on Work Incapacity

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Abstract

Work incapacity is a major public health challenge and an economic burden to both society and individuals. Understanding the underlying causes is becoming ever more relevant as many countries face an aging workforce. We examined stability and change in genetic and environmental factors influencing work incapacity from age 18 until retirement, and sex differences in these effects. The large population-based sample comprised information from 28,759 twins followed for up to 23 years combined with high-quality national registry data. We measured work incapacity as the total proportion of potential workdays lost due to sickness absence, rehabilitation and disability benefits. Structural equation modeling with twin data indicated moderate genetic influences on work incapacity throughout life in both men and women, with a high degree of genetic stability from young to old adulthood. Environmental influences were mainly age-specific. Our results indicate that largely the same genetic factors influence individual differences in work incapacity throughout young, middle and older adulthood, despite major differences in degree of work incapacity and probable underlying medical causes.

Keywords: Work incapacity; genetics; heritability; twin design; life course

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Incapacity to work due to physical or psychological health problems is a major public health challenge with substantial economic and social costs at both the societal and individual levels (Organisation for Economic Co-operation and Development [OECD], 2010). Most developed and many developing countries face an aging population (Harper, 2014; Hertel & Zacher, 2015), and a growing number of young adults receive disability benefits (Verhoof et al., 2012). This may lead to a lower number of workers per retiree and per benefit recipient and has made it a high political priority to maximize workforce participation. It is thus becoming ever more relevant to understand the underlying causes of work incapacity (subsequently used as a collective term for sickness absence, rehabilitation and disability pension) across the entire working age.

Medically certified illness or injury is, in most countries, a prerequisite for receiving health-related welfare benefits. Nevertheless, a variety of other factors also contribute to work incapacity, including demographic, psychosocial and work-related environmental factors (Allebeck & Mastekaasa, 2004; Dekkers-Sánchez et al., 2008). Factors affecting work incapacity can act at different stages in life and contribute differently to the development of work incapacity (Gravseth et al., 2007). However, research on the genetic and environmental mechanisms involved in the development of work incapacity is scarce (Harkonmaki et al., 2008; Narusyte et al., 2011). During the past decade, the role of genetic factors in explaining work incapacity has gained more attention. Genetically, informative studies enable one to disentangle genetic and environmental influences and estimate their relative importance in explaining individual differences in a phenotype (e.g., work incapacity). Recent, large-scale twin studies have shown that genetic factors explain a moderate-to-substantial percentage (33–66%) of the variance in sickness absence (Gjerde et al., 2013; Svedberg et al., 2012) and disability pensioning (Gjerde et al., 2013; Harkonmaki et al., 2008; Narusyte et al., 2011) in samples of different ages and from different countries. A 15-year follow-up study of Swedish twins aged from 35 until retirement age showed that genetic effects common to all ages explained one-third of the liability to disability pensioning, whereas almost two-thirds were explained by age-specific environmental factors (Narusyte et al., 2011).

Genetic influence on sickness absence and disability pensioning is likely to include genetic liability to health symptoms and disease, as well as genetic influences on psychological traits such as attitudes and personality that may affect selection into certain types of jobs, social contexts, or lifestyles associated with work incapacity (Allebeck & Mastekaasa, 2004; Ropponen et al., 2012; Virtanen et al., 2018).

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Demographic characteristics such as age and gender are regularly identified as strong predictors of work incapacity (Allebeck & Mastekaasa, 2004), with higher levels generally found among women and older age groups. In the present study, we aimed to (1) investigate the common versus age-specific genetic and environmental influences on work incapacity from young adulthood until retirement age and (2) test whether there were differences between men and women in the type, magnitude and stability of these influences.

Materials and Methods

Sample

The study is based on data from twins in the Norwegian Twin Registry (NTR), established in 2009 (Nilsen et al., 2016). The NTR consists of population-based Norwegian twin panels covering birth years 1895–1960 and 1967–1991 ($N = 40{,}639$ twins). For the present study, all twins born in 1926 and after who had given their consent to participate in health-related research and with known zygosity were included ($N = 29{,}257$). By using the unique national identification numbers issued to all Norwegians at birth, the data were linked to the Historical-Event Database (FD-Trygd) at Statistics Norway, containing longitudinal data for the entire population on labor-force engagement and social security benefits from 1992 and onwards. Data were also linked to the Cause of Death Registry administered by the Norwegian Institute of Public Health, containing dates and causes of all deaths in the population. As the register data at Statistics Norway are updated annually, we have obtained a detailed, longitudinal dataset, including annual information on sickness absence, medical and vocational rehabilitation, disability pension, work assessment allowance and employment status from 1992 until 2014. The data were reorganized according to a dynamic historical cohort design, covering the age range from 18 to 66 years (i.e., age of majority until year prior to pension qualifying age in Norway), with a maximum individual follow-up time of 23 years.

Zygosity was determined using validated questionnaire items (Magnus et al., 1983) and DNA analyses on a subgroup of the sample. For birth years 1926–1960, only same-sex twins were available. Individuals who had died in 1992 or earlier were excluded ($n = 498$), while individuals who died during the study period were coded as missing from the year of death. The final sample for analyses consisted of 28,759 twin individuals, including 5227 monozygotic (MZ) males, 7906 dizygotic (DZ) males, 6493 MZ females and 9133 DZ females. The Regional Ethical Committee approved the NTR and registry linkage.

Variables

Work incapacity was measured as the proportion of potential working days lost due to long-term sickness absence (exceeding 16 days), rehabilitation, work assessment, temporary disability and/or disability pensioning. This includes all available health/medical benefits covered by the Norwegian Insurance Scheme to compensate loss of income. We did not include sickness absence granted for pregnancy-related illness (chapter W in the International Classification of Primary Care; WONCA, 2005), due to potential impact on results and conclusions for all women (Sydsjö et al., 2001). Sickness absence among pregnant women is much more prevalent than among the total population of women in fertile age, and different risk factors from those influencing the general population seem to be involved (Dørheim et al., 2013; Seglem et al., 2017).

Sickness absences exceeding 16 days are covered by the mandatory Norwegian Insurance Scheme for a duration up to 52 weeks. Thus, the minimum sickness absence period recorded in this study was 17 days. Sickness absence and disability were registered with exact dates; thus, the exact number of days registered with each benefit could be calculated. Rehabilitation and work assessment allowance were registered by month, in which case we counted the person as absent the whole month. We approximated each month to contain 30.5 days and multiplied this by the number of months on the benefit. As employment is a prerequisite for sickness absence benefits, the potential number of working days is the number of contracted employment days. Rehabilitation, work assessment allowance and disability benefits do not require employment. Thus, the number of potential working days was equated with the number of days in a year (i.e., 365) for individuals on these welfare benefits. Proportions of work incapacity for each year ranged from 0 (no absence) to 100% (full-year absence).

Statistical Analyses

Data preparation. Prior to statistical analyses, we organized the data into five age intervals (18–29, 30–39, 40–49, 50–59 and 60–66). We first computed age by subtracting birth year from follow-up year. We then computed each individuals mean of annual work incapacity for each age period for which they had data, thereby accounting for individual differences in the number of years observed. Due to skewed distributions, the variables were natural log-transformed.

Biometric analyses. In the classical twin model, using information from MZ and DZ twin-pairs, individual differences in liability are assumed to arise from three latent factors: additive genetic influences (A), shared environmental influences (C) and nonshared environmental influences (E). MZ and DZ twin-pairs differ with respect to their genetic relatedness: MZ twins are genetically identical, while DZ twins share on average 50% of their segregating genes. When reared together, MZ and DZ twins share parts of their environment to the same extent (e.g., family's socioeconomic status). Consequently, additive genetic influences on a phenotype make MZ twins more similar to one another relative to DZ twins, whereas shared environmental influences make both types of twins more similar to one another (to the same extent). Nonshared environmental influences incorporate, by definition, environmental factors that make twins in the same family different from one another, including measurement error. Structural equation modeling of the variance (within-twin) and co-variance (across-twin) of a given phenotype allows for estimates of each of the variance components to be produced based on this information (Rijsdijk & Sham, 2002).

We applied a Cholesky decomposition, wherein phenotypic variances are decomposed into genetic, shared environmental and nonshared environmental components for each observed variable. When the variables (ACE model) are ordered in time, the Cholesky decomposition can be interpreted as a longitudinal model (Loehlin, 1996). Each genetic and environmental component can influence observations later in time, but not earlier. This means that the first observed variable in the model is influenced only by one set of A, C and E variance components, the second by the variance components influencing the first variable and a novel set of variance components, and so on (see Figure 1). The influence

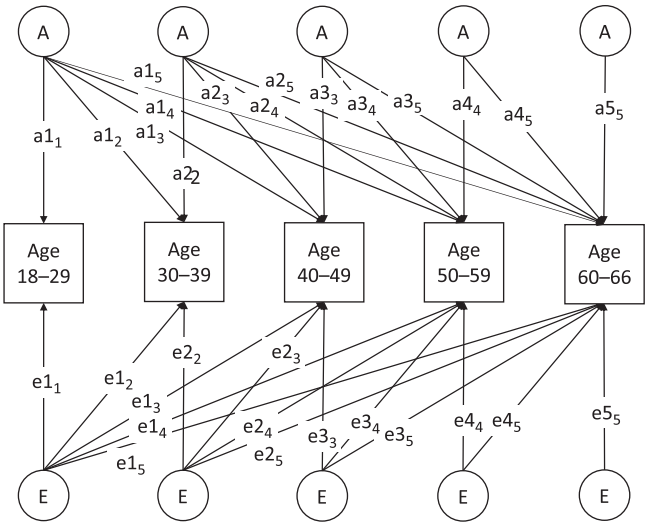

Fig. 1. Longitudinal Cholesky decomposition of work incapacity at different ages, with additive genetic (A) and nonshared environmental (E) effects.

of, for example, genetic factors in the ages 18–29 on variance in work incapacity at later ages can be interpreted as stability of genetic contributions.

Alternative models were compared to test for quantitative and qualitative sex differences. When there are quantitative sex differences, the same genetic and environmental factors influence the phenotype in both sexes, but their magnitudes differ. In contrast, when there are qualitative sex differences, a partially different set of genetic or environmental factors influence the two sexes. It was only possible to test qualitative sex differences among the youngest age groups, that is, 18–29, 30–39 and 40–49, as it is necessary to include opposite-sex twin-pairs. The models were fitted using Full Information Maximum Likelihood as estimation procedure to raw data in OpenMx 2.11.5 (Neale et al., 2016) within R 3.5.1. The raw data method utilizes all data, from both complete and incomplete pairs. The difference in −2 times the log-likelihood (Δ−2LL) is asymptotically χ^2 distributed, which allows testing for significant differences in χ^2 for nested submodels. In addition, we used the Akaike's Information Criterion (AIC; Akaike, 1987) and sample size adjusted Bayesian Information Criterion (ssaBIC; Sclove, 1987). By the principle of parsimony, models with the lowest AIC and ssaBIC values were preferred.

Results

Descriptive Statistics

Table 1 shows sample demographics and the number of twin-pairs for whom data were available at each age group. The change in mean work incapacity over time was quite large, increasing from an average of 2.6% and 4.0% per year in the youngest age group (18–29) to 32.5% and 39.3% in the oldest (60–66), for men and women, respectively (see Figure 2). Women showed significantly higher levels ($p < .001$) of work incapacity than men in all age groups. Phenotypic correlations (within-person, across-time) are reported in Table 2. The correlations, indexing the phenotypic stability of work incapacity, were generally large and slightly increasing in magnitude with age. Furthermore, correlations were highest between adjacent age groups.

Twin Correlations

MZ and DZ twin correlations within each age group are shown in Table 3. MZ correlations were consistently higher than DZ correlations, indicating additive genetic influences at all ages for both men and women. Particularly among women in the younger age groups (18–39) and among men in middle age (40–49), the DZ correlations exceeded half the size of the MZ correlations, suggesting that there may be influences of shared environment. For different-sex DZ twins (only available up until age 49), the correlations were generally lower than same-sex DZ correlations, indicating sex-specific etiological effects in terms of qualitatively different genetic or environmental factors.

Biometric Analyses

We began model testing to see if there were sex differences in the three youngest age groups (i.e., 18–29, 30–39, 40–49), as only these groups included opposite-sex twin-pairs. Compared to the qualitative sex difference model, the quantitative sex difference model did not indicate a statistically worse fit ($\Delta\chi^2 = 12.16$, $\Delta df = 6$, $p = .06$, $\Delta\text{AIC} = .17$, $\Delta\text{ssaBIC} = -27.3$). The AIC values were near equal, while the ssaBIC value was lower for the quantitative sex difference model. A model with no sex differences showed a worse fit than both models with sex differences (compared to the quantitative sex difference model: $\Delta\chi^2 = 518.08$, $\Delta df = 24$, $p \leq .001$, $\Delta\text{AIC} = 469.91$, $\Delta\text{ssaBIC} = 387.5$). Consequently, we continued with a model including quantitative sex differences in all five age groups, where we assumed that the same genetic and environmental components influence males and females, but to different degrees. Results from the multivariate Cholesky decomposition model fitting for all age groups are shown in Table 4. The better fit of a quantitative sex differences model compared to a model with no sex differences was confirmed with all five age groups. Furthermore, the small estimates of the C components could be set to zero without a significant deterioration of model fit. Thus, an AE model with additive genetic and nonshared environmental influences, and no shared environmental influences, was the final preferred model.

Standardized, squared path estimates for the longitudinal AE model with quantitative sex differences are presented in Table 5, along with 95% confidence intervals for the total variance components at each age. Genetic and nonshared environmental influences are grouped separately, each showing the specific factors that emerge in one age group and that show an effect at later ages (i.e., when reading down a column), indicating stability of contributions. Genetic factors originating in the ages 18–29 explained 45% of the variance in men and 42% of the variance in women at this age and explained a decreasing but substantial amount of the variance at later ages (decreasing from 27% and 25% at ages 30–39 to 18% and 21% at ages 60–66 in men and women, respectively). In contrast, nonshared environmental factors in the age group 18–29 had hardly any influence later on. The cross-sectional estimates of genetic and nonshared environmental influences at each age group can be read from each row and are summarized in separate columns showing the total heritability and nonshared environmental contribution. The total heritability estimates were moderate throughout working age in both men (ranging from 33% to 45%) and women (ranging from 35% to 45%), while the nonshared environment explained the remaining and larger share of the total variance in work incapacity.

The results are graphically illustrated in Figure 3 for men (top section) and women (bottom section). Stable genetic and

Table 1. Sample demographics and mean work incapacity by age group

Age group	Birth year[a], mean (range)	*N* Total	*n* Complete pairs	*n* Incomplete pairs	% Women	Mean (*SD*) men	Mean (*SD*) women
18–29	1978 (1967–1991)	11,588	4016	3556	59%	2.6 (9.6)	4.0 (11.2)
30–39	1968 (1953–1984)	13,633	5326	2981	56%	5.5 (16.7)	9.5 (21.4)
40–49	1957 (1943–1974)	15,908	6712	2484	53%	9.5 (23.4)	15.5 (29.2)
50–59	1948 (1933–1964)	14,852	6506	1840	51%	10.2 (24.1)	15.6 (29.3)
60–66	1943 (1926–1954)	12,742	5290	2162	51%	32.5 (42.4)	39.3 (44.5)

[a]Birth year instead of age because based on longitudinal data.

Table 2. Within-person, across-time phenotypic correlations for work incapacity in men and women

	Men				Women			
Age	18–29	30–39	40–49	50–59	18–29	30–39	40–49	50–59
18–29	–				–			
30–39	.67	–			.59	–		
40–49	.42	.72	–		.43	.72	–	
50–59	n/a	.53	.76	–	n/a	.50	.77	–
60–66	n/a	.36	.49	.78	n/a	.35	.54	.80

Note: All correlations were significant to $p < .01$; n/a indicates no available observations.

Table 3. Within-age group MZ and DZ twin-pair correlations for work incapacity

	Men		Women		Opposite sex
Age	MZ	DZ	MZ	DZ	DZ
18–29	.41	.18	.42	.27	.13
30–39	.36	.19	.34	.20	.09
40–49	.36	.22	.43	.22	.08
50–59	.40	.20	.40	.22	n/a
60–66	.38	.15	.36	.17	n/a

Note: MZ = monozygotic; DZ = dizygotic; n/a indicates no available observations.

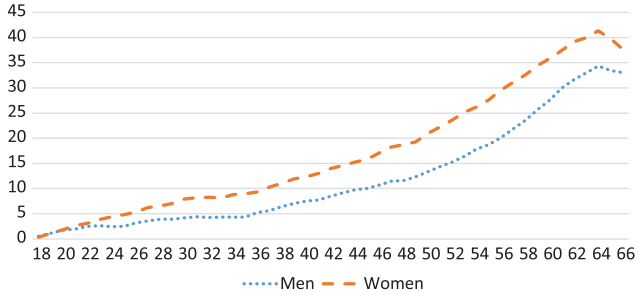

Fig. 2. Mean proportion of work incapacity across age for men and women (not including pregnancy-related sickness absence).

environmental contributions are indicated by early factors (lighter colors) continuing to account for a proportion of the phenotypic variance at later ages. New factors contributing to variance at later ages are represented by areas of darker color.

Discussion

This study is to our knowledge the first to examine stability and change in genetic and environmental influences on work incapacity throughout the entire working-age period, from age 18 until retirement. We used a twin design on data from a large population-based sample and found that genetic influences on work incapacity are moderate in magnitude and that much the same genes are influential throughout the working-age period. While nonshared environmental factors showed the largest contribution to individual variation in work incapacity, these factors had mainly short-term effects. The results indicated slight differences between men and women; heritable factors were of more importance for work incapacity in men than in women below the age of 40 and of more importance in women than in men after this age.

Over the working-age course, we observed a moderate-to-high stability of incapacity to work at the individual level. This phenotypic stability was largely explained by common genetic factors. For instance, more than half of the genetic variation in work incapacity (18 out of 33% in men and 21 out of 38% in women) at ages 60–66 could be explained by genetic factors already influencing work incapacity at ages 18–29. We were somewhat surprised by this finding, as many diseases contributing substantially to work incapacity, such as heart disease, cancer and respiratory conditions, typically have an age of onset from middle age and onwards. However, there are several plausible explanations for the relatively high stability of common genetic influences on work incapacity. First, many chronic and disabling conditions have an early onset. Mental disorders are a large diagnostic group in sickness absence and disability benefits, especially anxiety and depression (Henderson et al., 2011; Knudsen et al., 2013), which typically have an early onset (Kessler et al., 2007). There is a high rate of recurrence of sickness absence episodes granted for mental disorders (Koopmans et al., 2011), which frequently co-exists with physical or other mental illnesses, increasing the risk of work incapacity for both mental disorder and other reasons (Kessler et al., 2003; Torvik et al., 2014). Thus, the genetic influence on mental disorders is one reasonable explanation for the high stability of genetic influences on work incapacity from early to late adulthood. Second, the overall pattern of 'genetic stability, environmental change' is a typical finding in the field of behavioral genetics (Knopik et al., 2016). The striking parallel to our findings suggests that there may be a considerable behavioral component explaining individual differences in work incapacity and that genetically stable characteristics, such as personality factors (Turkheimer et al., 2014), may substantially influence work incapacity across age. Third, there is a moderate-to-substantial genetic component to various modifiable lifestyle factors linked to healthy aging (McGue et al., 2014). A recent large-scale, multicohort study concluded that lifestyle

Table 4. Model fitting statistics of quantitative versus no sex differences in work incapacity for total sample

No.	Models	−2LL	*df*	AIC	ssaBIC	Δ−2LL	Δ*df*	*p*	Comp. model
I	ACE – sex difference	154,336.7	61,499	31,338.7	154,979.8	–	–	–	–
II	ACE – no sex difference	154,754.0	61,544	31,666.0	155,107.7	417.27	45	<.001	I
III	**AE – sex difference**	**154,354.1**	**61,519**	**31,316.1**	**154,804.2**	**17.78**	**20**	**.602**	**I**
IV	AE – no sex difference	154,762.1	61,549	31,664.1	155,019.3	408.01	30	<.001	III

Note: −2LL = negative 2 log-likelihood; *df* = degrees of freedom; AIC = Akaike's information criterion; ssaBIC = sample size adjusted Bayesian Information Criterion; Δ−2LL = change in −2 log-likelihood; Δ*df* = change in degrees of freedom; Comp = comparison. Best fitting model is marked in bold.

Table 5. Standardized, squared path estimates and total variance components from best fitting model of work incapacity

	Genetic					Total	Nonshared environment					Total
Age	a1	a2	a3	a4	a5	h^2 [95% CI]	e1	e2	e3	e4	e5	e^2 [95% CI]
Men												
18–29	.45					.45 [.39, .50]	.55					.55 [.50, .61]
30–39	.27	.11				.39 [.34, .43]	.05	.57				.61 [.57, .66]
40–49	.19	.07	.12			.38 [.34, .42]	.01	.11	.50			.62 [.58, .66]
50–59	.18	.02	.10	.08		.38 [.34, .42]	.00	.06	.12	.44		.62 [.58, .66]
60–66	.18	.02	.02	.11	.01	.33 [.29, .37]	.00	.03	.07	.19	.39	.67 [.63, .71]
Women												
18–29	.42					.42 [.38, .47]	.58					.58 [.53, .62]
30–39	.25	.10				.35 [.31, .39]	.05	.60				.65 [.61, .69]
40–49	.23	.08	.15			.45 [.42, .48]	.01	.09	.44			.55 [.52, .58]
50–59	.21	.02	.12	.09		.44 [.41, .47]	.00	.05	.11	.40		.56 [.53, .59]
60–66	.21	.02	.02	.12	.01	.38 [.34, .41]	.00	.02	.07	.17	.36	.62 [.59, .66]

Note: a indicates additive genetic effects; h^2 indicates total heritability; e indicates nonshared environmental effects. Confidence intervals are likelihood-based.

matters for work incapacity, with indications that 15–31% of sickness absence days due to common diseases might be attributed to lifestyle factors such as physical activity, alcohol use, smoking and obesity (Virtanen et al., 2018). Thus, there may be common genetic factors explaining health behaviors early in life and disease outcomes later on.

Environmental factors unique to the individual, that is, not shared with the co-twin, and including measurement error, explained the largest share (55–67%) of individual differences in work incapacity, regardless of age and sex. This finding is in line with previous genetically informed studies on work incapacity measures (Gjerde et al., 2013; Harkonmaki et al., 2008; Narusyte et al., 2011; Svedberg et al., 2012). In contrast to genetic influences showing a high degree of stability, nonshared environmental factors were mostly age-specific. For example, individual-specific environmental factors explaining work incapacity in 30- and 40-year olds were mainly different. Substantial age group-specific environmental effects have also been found in previous twin studies of disability pension (Harkonmaki et al., 2008; Narusyte et al., 2011). The relatively short-term effects of the nonshared environment may partly be explained by the influence of sudden environmental events, such as accidents and traumas, but may also indicate that environmental exposures affecting work incapacity change as a function of age.

Our finding of moderate genetic influences on work incapacity in both men and women is in line with previous twin studies, with heritability estimates ranging from 36% to 49% in sickness absence (Gjerde et al., 2013; Svedberg et al., 2012) and 33–66% in disability pensioning (Gjerde et al., 2013; Harkonmaki et al., 2008; Narusyte et al., 2011). Two previous studies report a decrease in genetic influences on disability pensioning with increasing age, from ≤45 to 65 years in Finnish twins (Harkonmaki et al., 2008) and from ≤49 to 64 years in Swedish twins (Narusyte et al., 2011). Although our study is of a broader measure of work incapacity, the results are generally compatible with this, showing a decrease in heritability of work incapacity from middle to old working age. However, as the first longitudinal twin study on work incapacity to also include younger age groups (18–29 and 30–39), a more nuanced picture than just a decrease in total heritability across age is indicated, with different patterns in men and women.

We find that total genetic influences on work incapacity in men significantly decreased (as indicated by nonoverlapping confidence intervals) from 45% in the youngest (ages 18–29) to 33% in the oldest age group (60–66) and were stable between the ages of 30 and 59. A plausible explanation for the decrease in heritability is that heritable conditions lead to work incapacity early in life, while later in life it becomes more common with illness and health problems that are due to environmental stress and unfortunate coincidences, that is, nonshared environment. In women, there was a deviation from this trend. Heritability estimates decreased from ages 18–29 (42%) to 30–39 (35%), but then increased again. This was not expected and could be due to statistical fluctuations and multiple testing and should therefore be interpreted with caution. Possible speculative explanations include different use

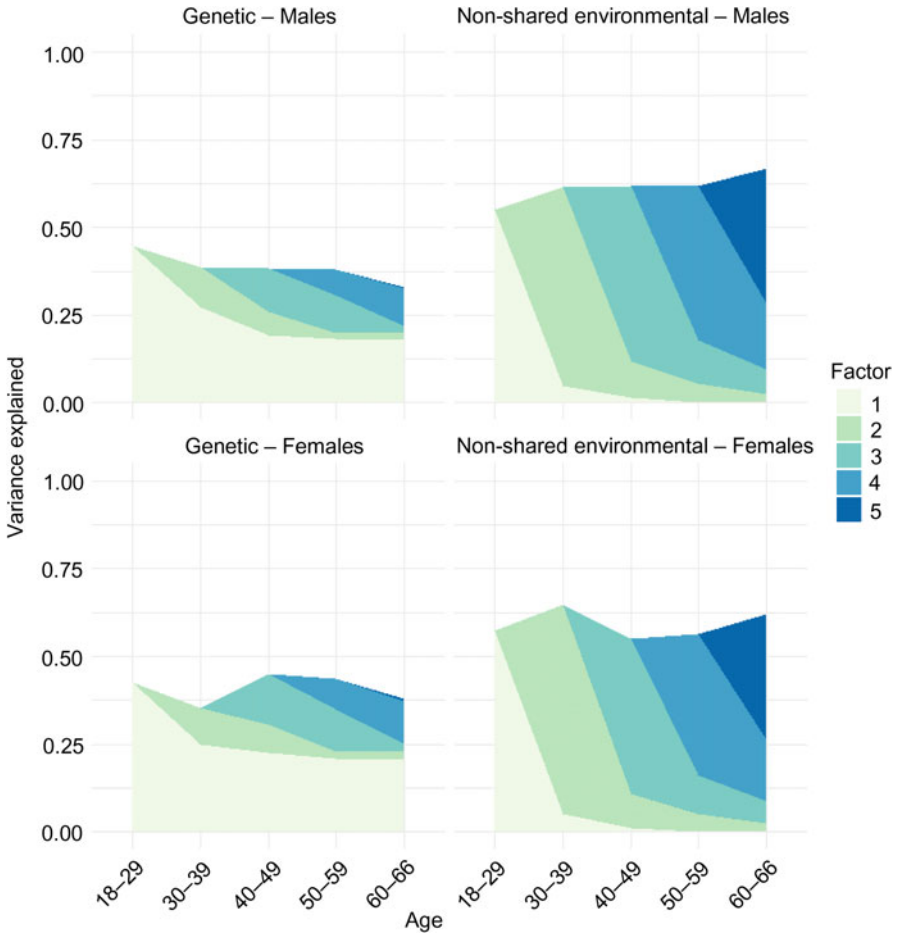

Fig. 3. Genetic (left section) and nonshared environmental (right section) influences on stability and change in work incapacity for men (top section) and women (bottom section). New factors contributing to variance at later ages are represented by areas of darker color.

of intervention strategies (i.e., environmental factors) in different age groups or that work-related environmental pressures build up at different rates in typical women's and men's professions. It could also be that the heritability of being in the labor market, and thus qualifying for sickness absence benefits, varies more between women's life stages, while employment is generally more stable for men across age groups. Previous twin studies of genetic and environmental influences on measures of work incapacity have either indicated no sex differences (Gjerde et al., 2013; Svedberg et al., 2012) or indicated the possibility of different sets of genes operating in men and women (Narusyte et al., 2011). It remains inconclusive whether and how genetic and environmental influences differ between men and women. The different results obtained so far may reflect variation in study population and context, as well as statistical power to detect such effects.

The strength of this article is the use of reliable and comprehensive population register data of all health-related absence benefits for a follow-up period of 23 years and covering the entire age span of the working-age population. Register data were linked via national identification numbers, thus, loss to follow-up or information bias was minimal or none. There are also some limitations of the study. First, contractual pension schemes may cause health selection effects among the oldest working ages. This was evident in the present study, with the mean proportion of work incapacity starting to decrease from age 64 even though the official pension age is 67. This may have underestimated genetic influences on work incapacity at later ages, as individuals with higher genetic liability to ill health may retire earlier. Second, higher correlations in same-sex twins than in different-sex twins suggest that there may be qualitative sex-specific genetic effects that we did not have enough power to detect. Third, the detection of shared environmental effect also requires high statistical power. Even in a large sample such as ours, nondetection of these effects does not mean that they do not exist. Fourth, we were unable to test sex differences in the oldest age groups due to lack of different sexed DZ twin-pairs. Finally, the study did not include diagnostic information. Thus, it is uncertain how the results generalize to specific disorders or health problems, and to what extent the results are driven by the composition of different disorders and diseases across the working-age course.

In conclusion, this study shows a considerable genetic contribution to the development of work incapacity throughout working age. Mostly different nonshared environmental factors influenced work incapacity at different ages, indicating short-term effects of environmental exposures. Future studies aiming to identify the specific factors that mediate genetic and environmental effects, as well as models of the relationship of genetic and environmental factors are needed in order to understand the complex mechanisms of work incapacity.

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Conflict of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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