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The rare disease neurofibromatosis 1 as a source of hereditary economic inequality: evidence from Finland

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Running title: Rare disease and economic inequality

Conflict of Interest

The authors declare no conflict of interest.

Abstract

Purpose: This study investigates whether individuals with neurofibromatosis 1 (NF1) fare worse than individuals without NF1 in terms of economic well-being. NF1 is relatively common in the population and provides an informative case of a rare hereditary disease.

Methods: We examined a subset of 692 individuals with verified NF1 from the Finnish total population-based NF1 cohort, and compared that to 7,407 control individuals matched for age, sex and municipality during 1997-2014. Economic well-being was operationalized with annual work earnings and total income including social income transfers.

Results: NF1 significantly worsened economic well-being. Low education, increased morbidity, and reduced labor market participation partly explained the effect of NF1. Yet, NF1 was independently associated with lower income even after adjusting for these factors. Further, NF1 had a larger negative effect on income from work than it had on total income, which indicates that the Finnish social security system partly compensated the labor market losses suffered by individuals with NF1. NF1 had a larger impact on economic inequality for men than women.

Conclusions: NF1 contributes to economic inequality. A hereditary disease may convey worse economic well-being over several generations.

Keywords

Neurofibromatosis, Nordic model, rare diseases, social income transfers, wages

Introduction

Although each rare disease has an incidence of less than 1/2,000, rare diseases affect, in total, 4-6% of the population globally.[1] It has been estimated that there are 27-36 million individuals with a rare disease in the European Union, and 25-30 million in the US.[2] Most rare diseases are heritable, life threatening, or chronically debilitating complex diseases. Although rare diseases vary in their clinical characteristics, patients share many experiences, such as difficulties in getting a diagnosis and in obtaining information about their disease, paucity of treatment options, poor resources for rehabilitation, and lack of peer support.[2] Although these shortcomings in health care services have been recognized, only little empirical research has been conducted on the effect of rare diseases on economic well-being and life in general. Carrying out large register-based studies on rare diseases is challenging, since collecting large datasets is impossible in the case of most rare diseases. The Finnish nationwide registers provide an excellent source for studying rare diseases. Neurofibromatosis 1 (NF1; OMIM 162200) was chosen as a model disease for this multidisciplinary study, as NF1 is sufficiently common to allow a case-control cohort study.

NF1 affects about 1 in 2,000-3,000 persons worldwide.[3,4] NF1 is a congenital multiorgan syndrome caused by pathogenic variants of the *NF1* gene.[5,6] NF1 has variable cutaneous, neural, and skeletal manifestations which may be present from infancy.[7] NF1 is associated with a 60% lifetime risk of cancer[8] and with significant excess mortality in all age groups.[3,4] Learning disabilities and cognitive and behavioral disorders are also common among individuals with NF1. A recent study found that NF1 is associated with reduced educational attainment, and the affected individuals have a tendency for vocational rather than academic educations.[9] Despite its specific characteristics, NF1 may point to aspects that need to be considered in the context of other rare diseases. For example, the tuberous sclerosis complex is a genetic disorder characterized by potentially disfiguring cutaneous manifestations, learning disabilities, and various tumors;[10] and the Lynch syndrome is associated with a similar level of cancer risk as NF1.[11]

Like many other rare diseases, NF1 is dominantly inherited, and approximately half of the individuals with NF1 have a parent with NF1. A sibling or a parent with NF1 may reduce a healthy family member's probability of obtaining academic education.[9] Moreover, the cognitive development and intelligence quotient (IQ) of children with familial NF1 may be inferior to those of individuals with sporadic disease.[12,13] It is therefore important to examine whether familial NF1 contributes to long-term labor market success.

The cost of illness of rare diseases has been studied from a societal perspective.[14] The effects of cancer and health shocks or the effects of disability on labor market performance and earnings in general have also been studied.[15–17] However, studies concerning the indirect individual costs in terms of reduced labor market performance or earnings of individuals with rare heritable diseases are scarce, or non-existent. This is also the case for NF1.

In order to better understand the effects of a rare, inherited disease on long-term labor market success and income inequality, we used the total population-based Finnish NF1 cohort and several nationwide registers to elucidate how NF1 affects labor market performance of individuals with familial or sporadic NF1 in the context of the Nordic model. By the Nordic model we refer to the societal model of the Nordic countries.[18] These countries share many characteristics, the most important of which in this context is the relatively high level of taxes and social income transfers. The aim of these policies is to moderate differences in disposable income.

Materials and methods

The study was approved by the Ethics committee of the Hospital District of Southwest Finland and research permissions were obtained from the Finnish Institute for Health and Welfare, Statistics Finland, and all participating hospitals. The study adhered to the principles set out in the Declaration of Helsinki.

Individuals with NF1 were compared to control individuals over a study period of 1997-2014. Individuals fulfilling the National Institutes of Health (NIH) diagnostic criteria for NF1 were identified by searching the 5 University Hospitals and 15 Central Hospitals of mainland Finland for NF1-associated hospital visits in 1987-2011. For this, the International Classification of Diseases (ICD), 9th edition code 2377A and ICD-10 codes Q85.00, Q85.0, Q85.09, Q85, and Q85.01 were used.[3] The medical records of each patient were reviewed to confirm that the NIH diagnostic criteria were fulfilled. The first NF1-related hospital visit was considered as the cohort entry. All analyses were restricted to persons aged 25-64, since most individuals within this age range have completed their studies but have not retired. Moreover, at least five years of data were required for each individual. A total of 692 individuals with NF1 fulfilling these criteria were identified, representing 594 different families. The NF1 syndrome was considered familial if a parent with confirmed NF1 was known, if familial disease was documented in the medical records, or if the individual with NF1 had at least one sibling with NF1.

For each individual in the full Finnish NF1 cohort, ten control individuals without NF1 matched for age, sex and municipality were retrieved from the Finnish Population Register Centre. The Finnish Population Register Centre keeps track of all inhabitants in Finland and records such data as date of birth, death and emigration, and all family relationships, e.g., parents, children, and siblings. By matching the controls with the NF1 cohort, the risk of bias related to temporal trends or the area of residence, such as the distance to health care service providers or educational institutions, was reduced. The cohort entry date of the respective individual with NF1 was used as the start of follow-up for the controls. First-degree relatives of individuals with NF1 were excluded from the control cohort. Consequently, none of the control individuals had a parent with known NF1. The final number of individuals in the control cohort was 7,407.

Five outcomes were studied:

1) The dichotomous indicator whether an individual earned any income from work during a year or not.
2) Among individuals who had income from work, the amount of income earned per year. Work income was deflated using the consumer price index provided by Statistics Finland to account for inflation and to allow comparability over the 18-year study period, and natural logarithm transformation was used to facilitate interpretation of the estimates.
3) The dichotomous indicator whether an individual had received social income transfers from the public sector or not. All transfers from the public sector during a year were included, except parental benefits. The transfers included items like pension income, unemployment benefits, study grants, sickness allowance and social assistance.
4) Among individuals with positive social income transfers, the amount of transfers per year. The amount of transfers was deflated using the consumer price index, and natural logarithm transformation was used.
5) The natural logarithm of the amount of total income per year, defined as the sum of the deflated work income and social income transfers.

The Finnish personal identity code was used as the key when information on work income, social income transfers, working months, days on sick leave and educational attainment were retrieved from Statistics Finland. The Finnish personal identity code is an immutable identifier assigned to each person at birth, and it is used to record information in the national population-based registries and for example in health care, thus allowing longitudinal follow-up with essentially no data loss. Hospital visits and hospital stays were obtained from the Finnish Care Register for Health Care which records all inpatient care and specialized outpatient care.

In all statistical models, individuals with and without NF1 were compared. All analyses were adjusted for sex, age, and the square of age to account for both linear and non-linear effects of increasing age.[19] In addition, models were constructed with adjustments for educational attainment, the number of hospital visits and hospital stays, as well as having inherited NF1, i.e., NF1 being familial or sporadic. The number of working months during the year was included in the analyses of annual earnings, amount of social income transfers, and total income. In the analyses of annual earnings and total income, the number of days on sick leave during the year was also accounted for. In terms of educational attainment, secondary education (International Standard Classification of Education, ISCED 3-5) and tertiary education (ISCED ≥6) were included as separate variables. The number of hospital visits and hospital stays during the year was included to account for NF1-related morbidity.

The follow-up of each individual ended at death, emigration, or the end of follow-up period in 2014, and the analyses always compare the individuals surviving to each age. The analyses were performed using linear panel data regression analysis which allowed quantification of the effect of NF1 on economic outcomes. The use of regression analysis makes it also possible to examine the contributions of education, labor market participation, and other pertinent confounders for explaining the association between NF1 and economic outcomes. Random effects were used to group the observations from different years of each individual. Thus, an observation is a person-year, and time (yearly) effects were controlled for. In all models, standard errors were further clustered within the strata of one individual with NF1 and the maximum of 10 matched control individuals to account for the matching of controls to individuals with NF1. The statistical analysis was conducted using Stata software version 15.

Results

A total of 692 individuals with NF1 and 7,407 controls were included in the analyses. 418 individuals had sporadic NF1 and 274 familial. While there were marked differences between individuals with NF1 and control individuals, there were also differences between individuals with sporadic and familial NF1 (Table 1). Individuals with familial NF1 were, on average, younger, and they had a lower age at the time of cohort entry than individuals with sporadic NF1. Individuals with familial NF1 had, compared to individuals with sporadic NF1, more hospital visits and stays, a higher likelihood of secondary education only and a lower likelihood of tertiary education.

Average work income and total income were lower among individuals with NF1 than among controls irrespective of age, while individuals with NF1 had received more social income transfers than controls (Figure 1). Regression analysis showed that having NF1 clearly affects labor market outcomes negatively: individuals with NF1 were less likely to earn work income and their annual earnings were lower compared to controls (Table 2). Accordingly, individuals with NF1 were more likely to obtain social income transfers and the amount of social income transfers per year was higher than among controls. There was no significant effect of the inheritance of NF1 on any of the outcomes in the models adjusted only for demographics. When the inheritance of NF1, morbidity, sickness absence, education, and labor force participation were accounted for, the effect of NF1 was attenuated but remained clearly significant (Table 2). As expected, morbidity, low education, and time outside the labor market were associated with decreased work income and increased income transfers. There was no difference between familial and sporadic NF1 in the fully adjusted models. Although the effect of NF1 was larger on annual work earnings than total income, NF1 did have a negative effect on total income (Table 2, columns 3-4 and 9-10). Models were also separately estimated for women (Table 3) and men (Table 4). The effects of NF1 on the outcomes were stronger for men than women. Among women, the effect of NF1 was largely explained by the adjustment factors included in the models, but a significant unexplained effect of NF1 remained among men.

Discussion

The research on rare genetic diseases has focused on the medical aspects of these conditions, while the economic consequences have gained only little attention. However, there is a growing body of literature on the effects of health problems on various labor market outcomes, such as employment and earnings.[20–22] Our results show that NF1 (a heritable multiorgan syndrome) impairs an individual's labor market performance and, thereby, economic well-being. NF1 decreases the probability of earning work income and decreases the amount of annual earnings among those with income from work (Table 2). Moreover, NF1 increases the probability that an individual receives social income transfers from the public sector and increases the amount of social income transfers received. The results concur with the expectations based on prior knowledge on the effects of NF1 on cognition, educational attainment and morbidity. Interestingly, our results suggest that the economic well-being of women is less impacted by NF1 than that of men (Tables 3 and 4). The reasons for the sex difference regarding the economic consequences of NF1 are an interesting avenue for further research.

Morbidity, in general, is well known to cause economic inequality. Our findings are indeed partly explained by the morbidity associated with NF1, leading to fewer years worked, fewer months of working per year and more frequent and longer hospital visits, circumstances which reduce work income and increase the need for social income transfers. Given the high cancer incidence related to NF1,[8] long sick leaves and early retirement may be more common among individuals with NF1 than among controls, although this assumption needs further research. Nevertheless, the effects of NF1 on an individual's socioeconomic situation are not completely explained by the associated morbidity, and the disorder also exhibits other mechanisms leading to decreased economic well-being. It is also possible that NF1-related morbidity contributes indirectly through, e.g., educational attainment.[9]

The effect of NF1 on labor market performance is partly due to attainment of less education by individuals with NF1 than control individuals. The lower educational attainment in NF1 has been previously reported.[9,23] The behavioral and cognitive problems associated with NF1[24–26] contribute to lower educational attainment,[9] and they may also play a direct role in working life. Attention deficits, hyperactivity, autism spectrum traits and lower IQ are all associated with NF1,[27–29] and it is plausible that they could also reduce work performance. The significant residual effect of NF1 persisting in the fully adjusted models may therefore be due to by these cognitive and behavioral characteristics of NF1, as well as to other factors, such as the disfigurement caused by NF1, i.e., benign cutaneous neurofibroma tumors that may hinder employment and social interaction. From a public policy perspective, improved education could also improve substantially the labor market performance of individuals with NF1.

Despite the previously reported effects of familial NF1 on cognitive development, IQ and educational attainment,[9,12,13] the inheritance of NF1 did not significantly affect labor market success. Having a parent with NF1 had no additional negative effect on labor market outcomes among individuals with NF1, although the NF1 syndrome, as such, conveys worse economic well-being and may thus be a genetic cause of multi-generational poor socioeconomic status. The mode of inheritance can guide support measures provided for individuals affected by genetic disorders. Further research on the effects of sporadic versus familial inheritance on non-medical outcomes is needed not only regarding NF1 but also other genetic disorders.

Our results show that having NF1 has a much larger negative impact on work income than on total income, because individuals with NF1 receive more social income transfers than controls (Table 2). This finding implies that extensive social income transfers provided by the Nordic welfare state protect to an important degree against health-related long-run earning losses. The insurance provided by the Nordic model is universal and automatic in the sense that the compensation mechanisms are not dependent on active decisions by individual citizens or their genes or environment. This provides potential efficiency gains over voluntary insurance systems, because it is very difficult for households to rationally track and assess the time varying probabilities that are related to health shocks that they face over their life course.

Social insurance provided by the Nordic model is, on the other hand, not complete in the sense that individuals with NF1 nevertheless do experience economic loss also in terms of total income.

In the present study, we verified the NF1 diagnosis of each individual with NF1 by reviewing their medical records and we used nationwide register data to retrieve information on labor market success and educational attainment. Follow-up of patients and controls was virtually complete. The use of register-based information on labor market success avoids bias associated with self-reported measures on labor market status and earnings. However, we inferred morbidity using the numbers of hospital visits and sick days and may therefore have missed part of the total morbidity treated in primary health care settings. The hospital-based ascertainment of the individuals with NF1 may have led to a higher likelihood of including individuals with severe disease manifestations into the cohort. We had no data on attention deficits, autism spectrum traits or lower IQ in the present cohort and could therefore not explicitly assess the contributions of these circumstances to the outcomes of interest. The use of a linear panel data regression with random effects to group individuals' observations from different years allowed longitudinal analysis of each individual and taking age into account. Since income evolves over lifetime, it is essential to allow for age-related changes. While the clustering of standard errors was used to account for the matching of individuals with NF1 and controls, within-family correlations were not accounted for, since we had no access to family relationships of the controls. The 692 individuals with NF1 came from 594 families.

Due to the specific characteristics of the labor market, and of the education and social support systems in each country, the results may not be generalizable to other countries and institutional contexts. Tuition-free education, public health care for all citizens and extensive social support are available in Finland, which arguably diminishes the differences between individuals with NF1 and controls, as suggested by the smaller effect of NF1 on total income than on work income. While the absolute income level and the relative contribution of social income transfers vary among countries, the major effect of NF1 *per se* and the contributions of low education and high morbidity are probably transferable between different developed societies. Further research is obviously required to quantitatively establish the economic consequences of NF1 outside the Nordic context. We are not able to ascertain whether the results of this study are due to labor market discrimination, which has been found to be the case in other settings.[30]

Conclusions

The results of this register-based multidiscipline study reveal a previously neglected association between NF1 and economic well-being. As a cancer syndrome, NF1 is life-threatening to the individual at hand, but its impact on the individual's ability to cope in the labor market may also extend negative consequences to the next generations. The findings are relevant for the care and for genetic counseling of individuals with NF1. Taking only the medical problems into account may be insufficient for optimal care. The results should inspire further research to examine means to support individuals with NF1, as both morbidity and cognitive difficulties associated with NF1 interfere with the individuals' ability to work. While the cognitive and behavioral problems and tumor types associated with NF1 are disease-specific, similar effects of morbidity, educational attainment and reduced number of working months may also be associated with other rare diseases.

Data Availability

Data are available upon request for researchers though data access is restricted. Please contact the Finnish National Institute for Health and Welfare and Statistics Finland for permission. Data can be requested from the corresponding author Prof. Juha Peltonen: Institute of Biomedicine, University of Turku, Kiinamyllynkatu 10, FI-20520 Turku, Finland; juhpel@utu.fi.

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Author Information

Conceptualization: all authors; Data curation: EJ, RAK, SP, JP; Formal Analysis: EJ; Funding acquisition: SP, JP; Investigation: all authors; Writing: all authors.

Ethics Declaration

The study was approved by the Ethics committee of the Hospital District of Southwest Finland and research permissions were secured from the Finnish Institute for Health and Welfare, Statistics Finland, and all participating hospitals. The study adhered to the principles set out in the Declaration of Helsinki. The study is register-based and retrospective and therefore exempt from obtaining informed consent from the participants.

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Figure legends

Figure 1. Work income (A), social income transfers (B) and total income (C) by age group among individuals with NF1 and controls.

Figure 1

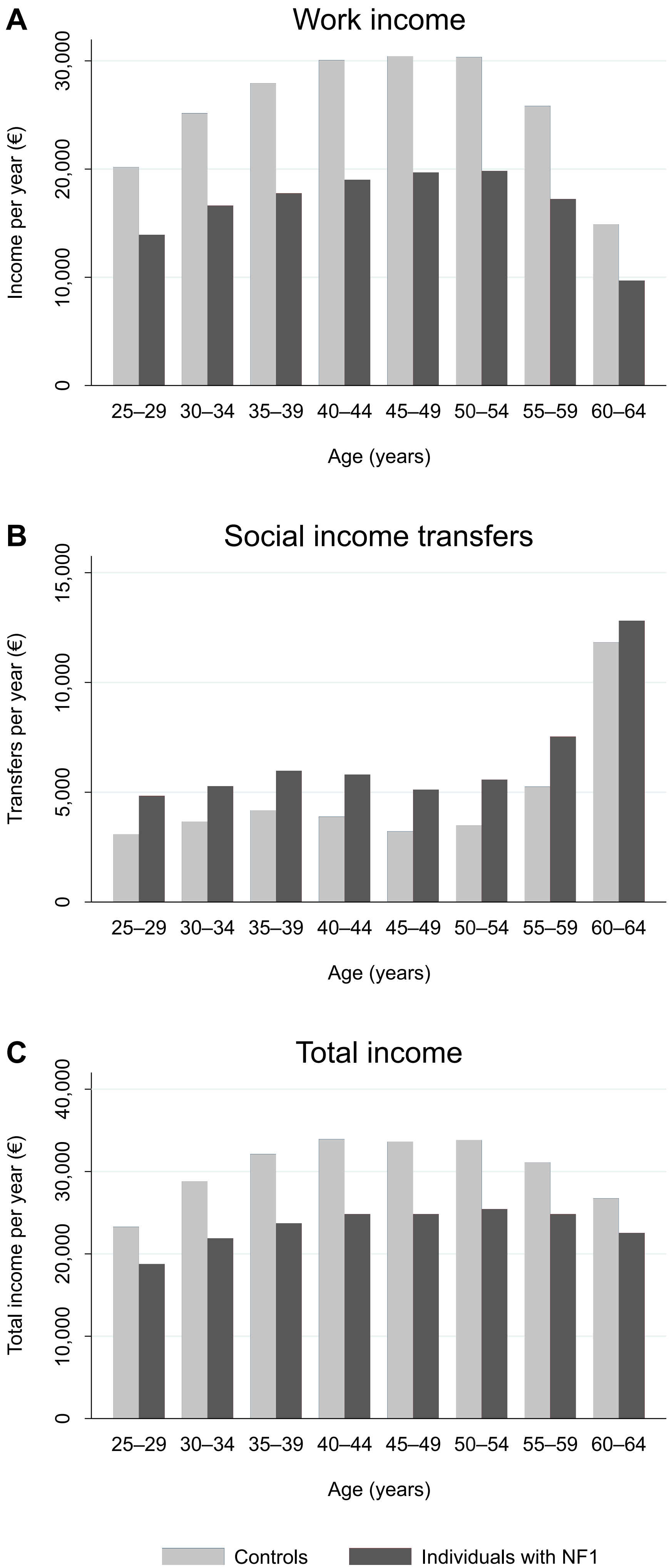
A
Work income
Income per year (€)
0
10,000
20,000
30,000
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
Age (years)
B
Social income transfers
Transfers per year (€)
0
5,000
10,000
15,000
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
Age (years)
C
Total income
Total income per year (€)
0
10,000
20,000
30,000
40,000
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
Age (years)
Controls
Individuals with NF1

Table 1. Characteristics of the NF1 and control cohorts.

	Sporadic NF1	Familial NF1	All NF1	Controls
N	418	274	692	7,407
Age (years), mean (SD)	43.99 (10.90)	40.00[b] (10.07)	42.44 (10.76)	42.59 (10.87)
Age at cohort entry (years), mean (SD)	34.23 (13.31)	29.42[b] (13.72)	32.36 (13.67)	32.02[a] (13.71)
Years in sample, mean (SD)	15.71 (3.55)	15.37 (3.75)	15.79 (3.51)	15.58 (3.63)
Females, % (N)	56 (234)	57 (156)	56 (390)	56 (4,148)
Months worked /year, mean (SD)	7.21 (5.47)	7.58[b] (5.35)	7.35 (5.43)	8.92[b] (4.82)
Number of hospital visits /year, mean (SD)	2.39 (5.06)	2.75[b] (6.23)	2.53 (5.55)	1.33[b] (4.52)
Number of sick days /year, mean (SD)	6.96 (30.38)	6.99 (31.31)	6.97 (30.74)	4.72[b] (23.86)
Any income earned, % (N)	70 (292)	73[b] (199)	71 (491)	84[b] (6,222)
Average annual work income, mean (SD)	17,127 (13,749)	17,115 (13,568)	17,123 (13,678)	26,151[b] (23,197)
Transfers received, % (N)	67 (280)	71[b] (195)	69 (475)	58[b] (4,296)
Average annual transfers, mean (SD)	6,235 (5,748)	5,891[a] (5,924)	6,102 (5,819)	4,336[b] (4,928)
Average annual total income, mean (SD)	23,375 (10,688)	23,007 (10,902)	23,232 (10,772)	30,491[b] (21,636)
Less than secondary education, % (N)	22 (92)	23 (62)	22 (154)	19[b] (1,407)
Secondary education, % (N)	57 (237)	63[b] (173)	59 (410)	44[b] (3,259)
Tertiary education, % (N)	21 (88)	14[b] (38)	18 (126)	37[b] (2,741)
Observations	5,996	3,807	9,803	107,147

[a] denotes differences in means that are statistically significant at the 5% level; [b] denotes differences in means that are statistically significant at 1% level;. Footnotes in column 2 indicate differences between sporadic NF1 and familial NF1. Footnotes in column 4 indicate differences between All NF1 and Controls.

Table 2: The effect of NF1 on labor market outcomes

	(1) Probability of earning work income		(2) Log of annual earnings		(3) Probability of obtaining positive amount of social income transfers		(4) Log of social income transfers		(5) Log of total income	
Individual has NF1	-0.131[c]	-0.119[c]	-0.305[c]	-0.111[b]	0.113[c]	0.064[c]	0.336[c]	0.104[b]	-0.199[c]	-0.047[a]
	(0.013)	(0.016)	(0.044)	(0.037)	(0.012)	(0.016)	(0.037)	(0.033)	(0.020)	(0.019)
NF1 x inherited NF1		0.022		-0.040		0.026		0.034		0.017
		(0.025)		(0.056)		(0.024)		(0.055)		(0.031)
Number of hospital visits / year		-0.003[c]		-0.007[c]		0.007[c]		0.001		-0.000
		(0.000)		(0.001)		(0.001)		(0.001)		(0.000)
Number of months working / year				0.170[c]				-0.126[c]		0.057[c]
				(0.002)				(0.002)		(0.001)
Number of sick days / year				-0.001[c]						0.000[c]
				(0.000)						(0.000)
Secondary education		0.155[c]		0.169[c]		-0.050[c]		-0.051		0.090[c]
		(0.011)		(0.021)		(0.010)		(0.028)		(0.013)
Tertiary education		0.206[c]		0.548[c]		-0.200[c]		-0.076[a]		0.432[c]
		(0.011)		(0.025)		(0.012)		(0.033)		(0.016)
Age	0.041[c]	0.039[c]	0.184[c]	0.078[c]	-0.028[c]	-0.025[c]	-0.119[c]	0.011[a]	0.112[c]	0.053[c]
	(0.002)	(0.002)	(0.006)	(0.004)	(0.003)	(0.003)	(0.008)	(0.006)	(0.003)	(0.002)
Age squared	-0.001[c]	-0.001[c]	-0.002[c]	-0.001[c]	0.000[c]	0.000[c]	0.002[c]	0.000	-0.001[c]	-0.000[c]
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Female	-0.016[a]	-0.024[c]	-0.336[c]	-0.327[c]	0.256[c]	0.269[c]	0.222[c]	0.289[c]	-0.221[c]	-0.238[c]
	(0.008)	(0.007)	(0.031)	(0.018)	(0.010)	(0.010)	(0.032)	(0.023)	(0.021)	(0.020)
N	116,950	116,950	96,886	96,886	116,950	116,950	68,502	68,502	115,252	115,252

Note: The data are model estimates with standard errors in parentheses. Observations are clustered within strata of 1 individual with NF1 and the maximum of 10 control individuals without NF1. The footnotes denote statistical significance: [a]: $0.05 > P \geq 0.01$; [b]: $0.01 > P \geq 0.001$; [c]: $P < 0.001$

Table 3: The effect of NF1 on labor market outcomes: women

	(1) Probability of earning work income		(2) Log of annual earnings		(3) Probability of obtaining positive amount of social income transfers		(4) Log of social income transfers		(5) Log of total income	
Individual has NF1	-0.134[c]	-0.116[c]	-0.258[c]	-0.023	0.069[c]	0.012	0.241[c]	0.028	-0.174[c]	-0.020
	(0.019)	(0.022)	(0.059)	(0.048)	(0.016)	(0.020)	(0.044)	(0.040)	(0.028)	(0.026)
NF1 x inherited NF1		0.013		-0.154		0.075[a]		0.076		-0.001
		(0.036)		(0.081)		(0.029)		(0.062)		(0.042)
Number of hospital visits / year		-0.003[c]		-0.008[c]		0.005[c]		-0.002		-0.002[c]
		(0.000)		(0.001)		(0.001)		(0.001)		(0.001)
Number of months working / year				0.171[c]				-0.112[c]		0.055[c]
				(0.003)				(0.002)		(0.001)
Number of sick days / year				-0.000				0.002[c]		0.000[c]
				(0.000)				(0.000)		(0.000)
Secondary education		0.168[c]		0.157[c]		-0.042[b]		-0.075[a]		0.068[c]
		(0.015)		(0.031)		(0.013)		(0.032)		(0.019)
Tertiary education		0.222[c]		0.557[c]		-0.139[c]		-0.068[a]		0.388[c]
		(0.016)		(0.035)		(0.014)		(0.033)		(0.022)
Age	0.049[c]	0.046[c]	0.186[c]	0.068[c]	0.000	0.003	-0.119[c]	0.015[a]	0.115[c]	0.052[c]
	(0.003)	(0.003)	(0.008)	(0.006)	(0.004)	(0.005)	(0.007)	(0.007)	(0.004)	(0.003)
Age squared	-0.001[c]	-0.001[c]	-0.002[c]	-0.001[c]	-0.000	-0.000	0.002[c]	-0.000	-0.001[c]	-0.000[c]
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
N	65,909	65,909	54,173	54,173	65,909	65,909	46,598	46,598	65,045	65,045

Note: The data are model estimates with standard errors in parentheses. Observations are clustered within strata of 1 individual with NF1 and the maximum of 10 control individuals without NF1. The footnotes denote statistical significance: [a]: $0.05 > P \geq 0.01$; [b]: $0.01 > P \geq 0.001$; [c]: $P < 0.001$

Table 4: The effect of NF1 on labor market outcomes: men

	(1) Probability of earning work income		(2) Log of annual earnings		(3) Probability of obtaining positive amount of social income transfers		(4) Log of social income transfers		(5) Log of total income	
Individual has NF1	-0.125[c]	-0.114[c]	-0.387[c]	-0.246[c]	0.174[c]	0.138[c]	0.452[c]	0.170[b]	-0.236[c]	-0.105[c]
	(0.020)	(0.025)	(0.069)	(0.060)	(0.020)	(0.026)	(0.072)	(0.056)	(0.035)	(0.031)
NF1 x inherited NF1		0.010		0.122		-0.043		0.001		0.085
		(0.040)		(0.079)		(0.039)		(0.101)		(0.049)
Number of hospital visits / year		-0.004[c]		-0.004[a]		0.010[c]		0.007[c]		0.002[c]
		(0.001)		(0.002)		(0.002)		(0.001)		(0.000)
Number of months working / year				0.165[c]				-0.156[c]		0.058[c]
				(0.003)				(0.003)		(0.001)
Number of sick days / year				-0.001[c]				0.003[c]		0.000
				(0.000)				(0.000)		(0.000)
Secondary education		0.102[c]		0.161[c]		-0.044[b]		-0.009		0.102[c]
		(0.014)		(0.028)		(0.016)		(0.042)		(0.018)
Tertiary education		0.147[c]		0.536[c]		-0.277[c]		-0.130		0.489[c]
		(0.015)		(0.035)		(0.018)		(0.068)		(0.024)
Age	0.031[c]	0.029[c]	0.183[c]	0.092[c]	-0.065[c]	-0.059[c]	-0.102[c]	-0.003	0.108[c]	0.057[c]
	(0.003)	(0.003)	(0.009)	(0.006)	(0.004)	(0.004)	(0.012)	(0.010)	(0.004)	(0.003)
Age squared	-0.000[c]	-0.000[c]	-0.002[c]	-0.001[c]	0.001[c]	0.001[c]	0.002[c]	0.000[c]	-0.001[c]	-0.000[c]
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
N	51,041	51,041	42,713	42,713	51,041	51,041	21,904	21,904	50,207	50,207

Note: The data are model estimates with standard errors in parentheses. Observations are clustered within strata of 1 individual with NF1 and the maximum of 10 control individuals without NF1. The footnotes denote statistical significance: [a]: $0.05 > P \geq 0.01$; [b]: $0.01 > P \geq 0.001$; [c]: $P < 0.001$