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## **Disability pension is associated with the use of benzodiazepines 20 years later – a prospective study**

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## **Abstract**

### **Objectives**

The Norwegian Government urges that actions are needed to stimulate the working capacity in disability pension (DP) recipients with such a potential. Identification of factors that may impair rehabilitation efforts, such as information on the start of benzodiazepines in DP recipients, may be useful information in this context.

Thus, the aim of the study was to describe the association between receipt of disability pension and later prescriptions of benzodiazepines among non-users at baseline.

### **Methods**

We followed a cohort reporting non-use of benzodiazepines, 6645 men and 6455 women aged 40-42 years who underwent health surveys in 1985 to 1989 in two Norwegian counties, with respect to subsequent use of benzodiazepines by linkage to the Norwegian Prescription Database for 2004-2006. At baseline, 83 men and 163 women reported to receive DP.

### **Results**

In both gender, the proportion started on at least one prescription of a benzodiazepine was about doubled among those reporting to be on a DP 20 years in the past, 21 % of all men and 29 % of all women, respectively.

Univariate odds ratio for a benzodiazepine prescription for men and women on a DP were 2.6 (95% CI 1.5- 4.4) and 2.1 (1.5-2.9), respectively, as compared with those not receiving a DP. After adjustment for alcohol, smoking habits, physical activity, socio-economic and health variables, the odds ratios was lowered for both sexes, being 2.1 (1.2-3.7) (men) and 1.6 (1.1-2.3) (women).

### **Conclusions**

For both men and women the chance of being prescribed benzodiazepines was higher among those reporting to DP recipients 20 years in the past.

**Key words:** employment status, disability pension, benzodiazepines, longitudinal studies, pharmacoepidemiology, prescription database, Norway

## **Background**

Despite above average life expectancy, Norway has a higher share of people on disability benefits, than most other OECD countries [1]. As a result, 11 per cent of the working population (18-67 years) received a disability benefit in Norway in 2006 [2]. In Norway, an insured (National Insurance Scheme) person between 18-67 years, whose working capacity is permanently reduced by 50 per cent due to illness, injury or defect is entitled to a disability benefit. Today, two different disability benefit schemes exist in Norway: time limited disability benefit and disability pension. Traditionally a disability pension was granted on a permanent basis. However, during the last decade The Norwegian Government have introduced several policy changes to arrest the upward trend; the time limited disability benefit including follow-up by The Norwegian Labour and Welfare Service (NAV) was introduced to prevent claims of permanent disability pensions. In addition, initiatives aiming at the reintegration into the labour market of those already on a disability pension have been launched. The Norwegian Government urges, however, that further actions are needed to stimulate the working capacity in disability pensioners with such a potential.

Several cross-sectional studies have shown that non-participation in the labour market seems to be associated with more frequent use of anxiolytics, hypnotics and/or benzodiazepines [3-7]. This association is, however, difficult to interpret in cross-sectional studies. The higher use among those not employed may, on one hand, be explained by drug use as a proxy of mental illness, the precipitating reason for disability in the first place. On the other hand, and irrespective of the precipitating cause of disability, it is reasonable to believe that being on a disability pension may be associated with a number of psychological problems caused by, for instance, social isolation. Thus,

drug treatment with anxiolytics, hypnotics and benzodiazepines may be initiated to relieve these symptoms.

It is well accepted that, even at therapeutic doses, benzodiazepines are capable of causing physiological and pharmacological dependence leading to withdrawal syndrome after cessation of use [8]. In addition, benzodiazepines impair psychomotor skills and cognitive functions, interfering with people's daily functioning [9] .Thus, initiation of benzodiazepines among disability benefit recipients might lead to a further impairment of health and rehabilitation efforts, contributing to a consolidation of the disability situation. Interestingly, randomised controlled trials have shown that withdrawal from benzodiazepines give significant better psychomotoric function compared to the control group remaining on benzodiazepines [10, 11].

The Norwegian Government urges that large efforts will be needed to bring those of the disability pensioners who are able to work into employment. Identification of factors that may impair rehabilitation efforts, such as information on the initiation of benzodiazepines in DP recipients, may be useful information in this context.

## Aims

To our knowledge, the epidemiology of incident drug-taking behaviours in general, and use of benzodiazepines in particular, among disability pensioners are scarcely described in the literature. A longitudinal design, with data from the Norwegian health surveys in 1985-1989 linked to data from a prescription database in 2004-2006, was used to investigate the association between the receipt of disability pension among 40-42 year old non-users of benzodiazepines and prescriptions of benzodiazepines 20 years later, a span covering a larger part of the potential active workforce period.

## **Material and methods**

### *Health surveys-information on independent variables*

All men (15 606) and women (14 748) aged 40-42 in the two Norwegian counties of Østfold and Aust-Agder were invited to participate in a population-based health survey organised by the National Health Screening Service, and has been described earlier [12-14]. The health survey was directed toward cardiovascular disease. Two examinations targeting two different generations of 40-42 years at the time of survey were carried out with three years interval both in Østfold (1985 and 1988) and in Aust-Agder (1986 and 1989). The total response rate was high; 72 % for men and 81 % for women.

The participants completed a self-administrated questionnaire covering different sociodemographic-, health- and lifestyle variables such as disability status, smoking, physical activity and others. A physical examination comprised measurements of weight, height, blood pressure. At the examination site an additional questionnaire was handed out to be filled out at home and returned by mail. All participants who where medically examined received this questionnaire. The response rate was 82 %. The questionnaire included separate questions covering alcohol use, use of analgesics, anxiolytics or hypnotics. In addition, in the surveys in 1988 and 1989 (and therefore a sub-sample of our study population), the second questionnaire included a question regarding nervous or mental health problems as told by the doctor. Details from the questionnaire, from which the variables are defined, are described in Table 1.

We excluded from our study persons who died or emigrated from Norway (451 men and 326 women) before January 2004 (Figure 1). In a second step we removed all those who received drugs reimbursed due to cancer diseases defined as the code §9.9 in the reimbursement scheme (93 men and 80 women).

Further, to study incident use of benzodiazepines we excluded current users at baseline. The participants answered whether they used anxiolytics or hypnotics in one question which did not distinguish between these two drug classes (Table 1). Benzodiazepines represented 99 % of all sale anxiolytics/hypnotics in 1980ies in Norway and therefore anxiolytic/hypnotic users will be referred to as benzodiazepine users [15]. A majority of 6645 men and 6455 women were defined as nonuser of benzodiazepines at baseline in

1985-89 according to this definition, and these persons were followed up with respect to subsequent prescription of benzodiazepines in 2004-2006. Parallel, among the participants who had received a questionnaire including a question regarding mental health symptoms, 3660 men and 3261 women were followed up with respect to subsequent prescription of benzodiazepines in 2004-2006.

In addition to disability status, several other factors associated with the use of benzodiazepines were included in our analysis; age, gender, alcohol consumption and smoking habits, marital status, physical activity, use of analgesics, somatic (cardiovascular morbidity) and nervous/mental health problems. See Table 1 for details on questions and variable definition. Analgesics users were defined as persons who answered they had used analgesics daily or every week during the last month (Table 1). Persons who used analgesics less than every week were defined as non-users according to probable common monthly use of analgesics among women due to menstrual pain. Analgesics use was defined in the same way for men.

#### *Norwegian Prescription Database (NorPD) - information on dependent variables*

Prescription data about benzodiazepines in 2004-2006 were drawn from the NorPD which covers the entire nation (4.6 million inhabitants) [16]. From 1 January 2004 all the pharmacies in Norway became legally obliged to send in all electronic data on prescriptions. These returns are sent to the Norwegian Institute of Public Health. NorPD contains information of all individuals who have received prescription drugs dispensed at pharmacies. All prescriptions reimbursed or not, are stored in the database. The drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification system [17]. The data collected for our study were patients unique identifying number

(encrypted), sex, age, the date of dispensing, and drug information (brand name, package size, number of packages, ATC-code, Defined Daily Dose (DDDs), price). The code of reimbursement is also recorded and this may function as a proxy of diagnosis. Code §9.9 is dedicated to cancer diseases.

The benzodiazepines were defined by the ATC-code N05BA and N05CD in the ATC-classification system. Use of benzodiazepines was defined as at least 1 prescription of a benzodiazepine during study period 1 January 2004 - 31 December 2006.

In addition, and among benzodiazepine users, the amount of benzodiazepines during the same period in terms of total DDDs was analysed.

Data from the health surveys and NorPD were linked based on the unique 11-digit identification number, assigned to all individuals living in Norway.

## Statistics

Chi-square test was used to assess equality of proportions across the groups of drug use. Fishers exact test were used when the expected count in cells were less than 5. Mann-Whitney test was used for variables with a skewed distribution. Odds ratio (OR) with 95 % confidence intervals (CI) were estimated separately for men and women by logistic regression. All analyses were done using SPSS 16.0 for Windows. Level of significance was set to  $p < 0.05$ .

## Ethical considerations

The study protocol was assessed by the Regional Committee for Medical Research Ethics and approved by the Norwegian Data Inspectorate. The study has been conducted in full accordance with the World Medical Association Declaration of Helsinki.

## Results

Characteristics of the study population, non-users of benzodiazepines at baseline, are shown in table 2. The proportion of 40-42 year old individuals reporting to be receivers

of a disability pension was about doubled in women (N=163; 2.5%) as compared to men (N=83; 1.3 %) (Table 2). There was a higher prevalence of teetotallers, current daily smokers (women only), and physically inactive persons among receivers of a disability pension. There was also a higher prevalence of unmarried, cardiovascular history, and use of analgesic drugs among those reporting to be on a disability pension.

In both gender, the proportion who received at least one prescription of a benzodiazepine 20 years later was about doubled among those reporting to be on a disability pension when aged 40-42 in 1985-89, 21 % of all men and 29 % of all women, respectively (table 2). Further, median DDD of benzodiazepines retrieved among users during the study period were increased, but not significantly, among receivers of a disability pension in both gender, 50 versus 30 DDD respectively (table 2).

Univariate OR for incident use of benzodiazepines among disability pensioners were 2.6 (1.5-4.4) in men and 2.1 (1.5-2.9) in women, respectively, as compared with those reporting to be non-receivers of a disability pension 20 years in the past (table 3). After adjustment for lifestyle, health, and socio-economic variables the OR was lowered for both sexes, being 2.1 (1.2-3.7) (men) and 1.6 (1.1-2.3) (women).

Adjustment for nervous or mental health problems as told by the doctor was possible only in a sub-sample of the study-population who had answered this question.

In gender specific analyses, adjustment for mental health problems at baseline gave a higher OR for benzodiazepines 20 years later in male disability pensioners (2.6 (1.3-5.5)). The same trend was observed among women, however the OR for later benzodiazepines became non-significant (OR 1.4 (0.8-2.2)). Overall, adding adjustment for mental health problems and gender into the multivariate analysis, revealed an OR for benzodiazepines among receivers of a disability pension of 1.6 (1.1-2.5).

## Discussion

The proportion that had started benzodiazepines, were doubled in those reporting to be disability pensioners at the age of 40-42, compared to those reporting not to be on a disability pension at baseline.

Our results may to some extent reflect what is generally well known; that BZD use increases with age. However, our design, comparing incident BZD use in DP recipients with the remaining population, highlight that excessive incident BZD use may be attributed to the DP situation. This observation was supported by our multivariate analysis where the receipt of a disability pension had an independent effect on incident use of benzodiazepines 20 years later, after controlling for alcohol, smoking habits and several other potential confounders. In Norway, and other OECD countries, mental health disorders and musculoskeletal problems are the main reasons for disability benefit claims [2]. Further, cross-sectional studies have disclosed that mental health factors, anxiety disorders in particular, predicts benzodiazepine use [7]. A higher incidence of benzodiazepine use among those reporting to be on a disability pension may be explained by a higher prevalence of mental health symptoms in this group at baseline. However, adjusting for nervous/mental health problems, as told by the doctor, in a sub-group of our study population, still revealed an independent effect of self-reported disability pension on use of benzodiazepines 20 years later, most pronounced in men. Obviously limitations in using this variable to adjust for mental illness at baseline exist, and the results should be interpreted with caution. A discrepancy between the actual mental symptom load and the individuals response to this question may be caused by several factors such as; the respondents recall, the subjective interpretation of the physician `s message, as well as interpretation of the question in the questionnaire.

It is a general observation that there exist two female BZD users for every male user of BZDs, as reflected in prescription data among 60-69 year old as well as in the total Norwegian population [18]. Obviously, more women are started on BZDs, as reflected in our results as well. The non-significant interaction supports the view that the risk ratio (or

odds ratio) between women and men in being prescribed a BZD is the same in people receiving and people not receiving a disability pension.

A limitation of our study is the description of use of benzodiazepines according to self-reported disability status 20 years in the past. The proportion on a disability pension increases with age; e.g. in 2006 about 25% of all men and 37 % of all women aged 60 years in Norway were receivers of a disability pension, as compared to 1-2% of the 40-42 year old participants in our study [2]. Thus, an unknown number of the initially non-disabled 40-42 years old will have changed their disability status during this period. In this situation, the OR estimates as presented will be underestimated, and biased towards the null.

Another limitation is that no information is available on use prior to the period covered by the questionnaire or in the 20 year lasting period between the two measurement points. It may very well be that some of the current users also used benzodiazepines regularly or in periods preceding the presentation of the questionnaire. Further, in this study benzodiazepine use is defined according to the retrieval of *one* prescription of a benzodiazepine during a three years period. In Norwegian recommendations benzodiazepines are recommended for short-term use only, up to 2-4 weeks, in treatment of severe anxiety and insomnia [19]. One prescription of a benzodiazepine is neither an outcome for long-term use, nor an addictive use pattern, and should be interpreted with caution.

In the present study we chose to focus on later prescriptions of traditional benzodiazepines, with its well known potential of causing addiction problems and other negative effects interfering with people's daily functioning [8, 9]. Thus, we excluded prescriptions on benzodiazepine-like hypnotics from our analysis. In Norway benzodiazepine-like hypnotics are now recommended as first-choice hypnotics for short-term use in severe insomnia. These substances, zopiclone in particular, are the most commonly used hypnotics in Norway. Hence, about 90 % of all 60-69 years olds who

retrieved at least one prescription on a hypnotic in Østfold an Aust-Agder in 2006 were users of benzodiazepine-like hypnotics [18]. Recent literature, however, adds to the growing evidence that these substances have a similar potential for negative effects as traditional benzodiazepines [20-22]. Still we wanted to restrict our analysis to the prescription of the traditional benzodiazepines, which constitute a better documented marker of an addictive use pattern [14, 20, 23].

This study is prospective with a nationwide register as an end-point, which implies minimal risk of selection or information bias. Another strength of our study is the narrow age range, since age as an important confounder is taken into account in the design. However, we cannot assess whether these findings are valid for other age-groups. Further, even if many potential confounders associated with prescription of benzodiazepines are registered, not all possible confounders could be taken into account. For example, we do not know the indication for later prescriptions of benzodiazepines. No evaluation of the non-attendees was performed in this study. However, receivers of disability pension were over-represented among the non-attendees in a parallel Norwegian health survey [24]. Lower attendance of disability pensioners, presumably with poorest health, will most likely have biased our OR estimates towards null.

In conclusion, this prospective study provides evidence of an increased risk of the initiation of benzodiazepines among those reporting to be disability pensioners 20 years in the past. The limitations with our study-design do not allow us to conclude neither on long-term use or an addictive use pattern, in which there is a particular concern regarding the negative effects of benzodiazepines interfering with people's daily functioning [9]. However; about 20% of all men and 30% of all women reporting to be disability pensioners at the age of 40, had started benzodiazepines 20 years later, a period covering most of their potential workforce period.

Being on a disability pension may be a positive alternative to join the workforce. However, many disability pensioners perceive their disability situation as passive,

unwanted and experience themselves as being excluded from the strong social and personal values associated with being a part of the workforce [25]. Reintegration into the labour market of disability pensioners with a working capacity has been an important part of the political agenda in Norway the last decade. Our findings may highlight the need of further research in this area. More detailed information on the use pattern of benzodiazepines among disability pensioners are needed to make conclusions on "problematic" use, with a potential to add up as yet another factor contributing to a consolidation of the disability situation.

### **Conflict of interest**

None of the authors have any conflict of interests.

### **Acknowledgement**

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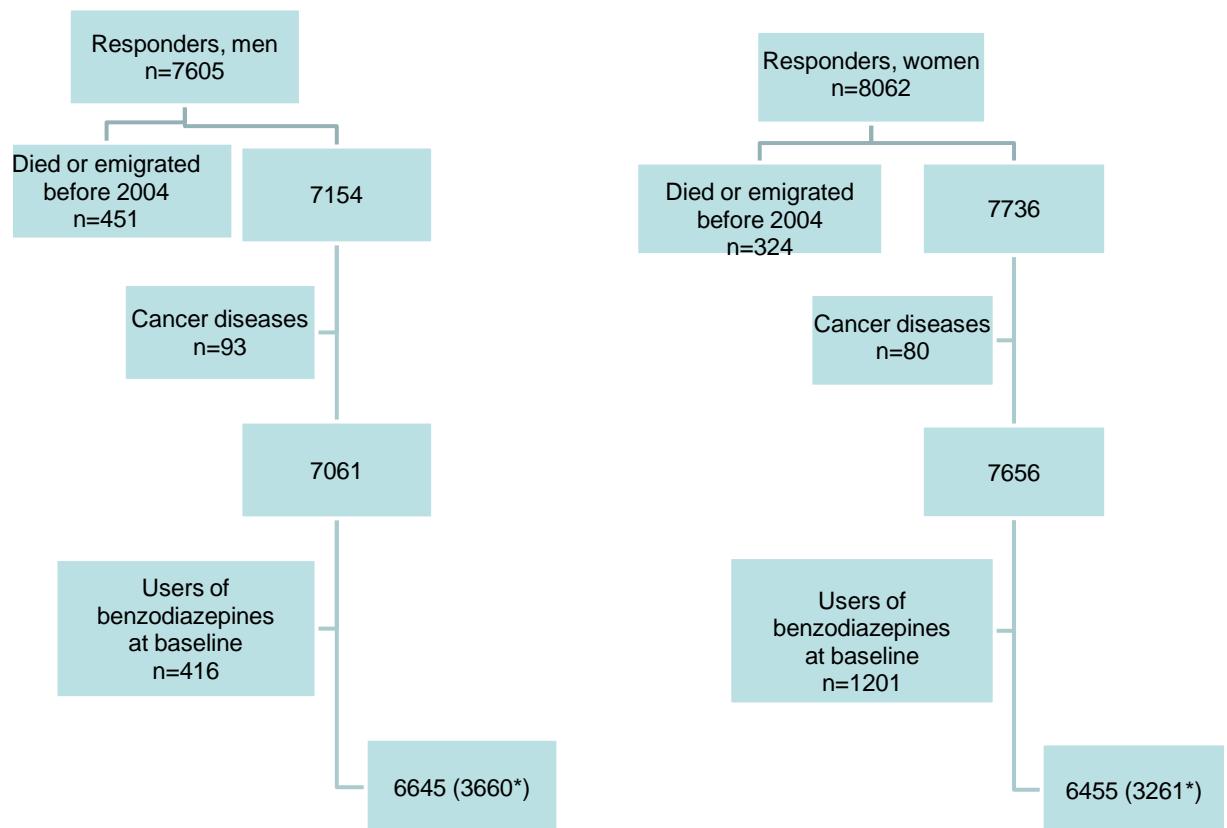
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Figure 1. Flow chart for the study population. Health surveys in Østfold and Aust-Agder (1985-89)



\*participants in 1988-89; sub-sample of the study-population who had received and answered a questionnaire including a question regarding nervous or mental health problems as told by their doctor.

Table 1. Questions and variable definition on drug use and other factors with answering alternatives used in the health survey in Østfold (1985 and 1988) and Aust Agder (1986 and 1989).

<b>Self-administered questionnaire</b>	<b>Answering alternatives</b>	<b>Variable definition</b>
<b>Anxiolytics/hypnotics*</b>		
How often have you used anxiolytics or hypnotics during last month?*	Daily (1); every week, but not daily (2); less than every week (3); not used during last month (4)	Users = 1-3; non-users = 4
<b>Analgesics</b>		
How often have you used analgesics during last month?	Daily (1); every week, but not daily (2); less than every week (3); not used during last month (4)	Users = 1,2; non-users = 3,4
<b>Alcohol consumption habits</b>		
How often have you drunk beer, wine or spirits during the last 14 days?	Teetotaller (1); not during the last 14 days, but are not a teetotaller (2); 1-4 times (3); 5-10 times (4); > 10 times (5)	Teetotaller =1; normal drinker =2,3; problem drinker=4,5
<b>Smoking habits</b>		
Do you smoke daily at present?	Yes (1)/no (2)	Smokers =1; ex-smokers= 3; non-smokers =2,4
Did you smoke earlier?	Yes (3)/no (4)	
<b>Physical activity</b>		
Describe the physical activity in your spare-time, on average during the last year.	Description of four levels of physical activity, sedentary to intense, in spare time.(1-4)	seldom/never physical active =1; active =2-4
<b>Cardiovascular symptoms</b>		
Previous MI, angina, stroke, diabetes	Yes (1)/no (2)	CVD history =1 or 3 ; no CVD history = 2 and 4
Descriptions of symptoms	Yes (3)/no (4)	
<b>Working status</b>		
Do you receive full or reduced disability pension?	Yes (1)/no (2)	Receivers of a disability pension=1; non-receivers =2
<b>Mental health problems**</b>		
Have you ever been told by your doctor that you have nervous or mental health problems?	Yes (1)/no (2)	nervous/mental health problems=1; non-presence=2

\* 99% of anxiolytics/hypnotics sale in Norway in 1989 were benzodiazepines.

\*\*Only included in the questionnaires in health surveys in 1988 and 1989

Table 2. Baseline characteristics for men and women aged 40-42 years which were nonusers of benzodiazepines when surveyed in 1985-1989. Use of benzodiazepines retrieved from the Norwegian Prescription Database in 2004-2006.

	Men			Women		
	Disability pension (1985-1989)		p	Disability pension (1985-1989)		p
	Yes (N=83)	No (N=6553)		Yes (N=163)	No (N=6284)	
<i>Baseline characteristics 1985-1989</i>						
Alcohol habits						
Teetotallers	17 (21.5)	579 (8.9)		42 (26.1)	1102 (17.6)	
Normal consumption	57 (72.2)	5273 (80.8)		114 (70.8)	4891 (78.3)	
High consumption	5 (6.3)	673 (10.3)	***	5 (3.1)	256 (4.1)	*
Smoking habits						
Current daily smokers	42 (50.6)	2608 (39.8)		74 (45.4)	2176 (34.6)	
Ex-smokers	23 (27.7)	2124 (32.4)		49 (30.9)	2120 (33.7)	
Non smokers	18 (21.7)	1821 (27.8)	0.132	40 (24.5)	1988 (31.6)	*
Seldom/never physical active	28 (34.1)	1269 (19.4)	***	60 (36.8)	1350 (21.5)	***
Married	51 (61.4)	5732 (87.6)	***	108 (66.3)	5462 (87.0)	***
Cardiovascular history	10 (12.0)	340 (5.2)	**	20 (12.3)	290 (4.6)	***
Analgetics use	15 (18.1)	225 (3.4)	***	48 (29.4)	500 (8.0)	***
<i>Prescription of BZDs in 2004-2006<sup>a</sup></i>						
Use of benzodiazepines (%)	17 (20.5)	602 (9.2)	***	48 (29.4)	1059 (16.4)	***
Median DDD (IQR) among users	50 (25,160)	30 (13,120)	0.189	52 (13,265)	30 (10,100)	0.059
% > 100 DDD among users	5 (29.4)	159 (26.4)	0.781	15 (31.3)	244 (23.0)	0.189

\*p-value<0.05; \*\*p-value<0.01; \*\*\*p-value<0.001

<sup>a</sup>use/users of BZDs was defined as the retrieval of at least 1 prescription of a BZD (N05BA/N05CD) during study period 2004 - 2006

Table 3. Association between receipt of disability pension in 1985-1989 with incident prescription of benzodiazepines in 2004-2006. Unadjusted and adjusted odds ratio (OR) with 95% confidence intervals.

	Men		Women	
	Prescription of benzodiazepines in 2004-2006		Prescription of benzodiazepines in 2004-2006	
	Unadjusted OR (95% CI)	Multivariate* OR (95% CI)	Unadjusted OR (95% CI)	Multivariate* OR (95% CI)
Disability pension in 1985-1989				
No - reference	1.0	1.0	1.0	1.0
Yes	2.6 (1.5-4.4)	2.1 (1.2-3.7)	2.1 (1.5-2.9)	1.6 (1.1-2.3)

\*adjusted for alcohol habits, smoking habits, physical activity, marital status, cardiovascular symptoms and use of analgesics

