Social inequalities in use of potentially addictive drugs in Norway – use among disability pensioners

Ingeborg Hartz[1], Aage Tverdal[2] and Svetlana Skurtveit[2,3]

1) Department of Health and Sports, Hedmark University College, Kirkeveien 47, 2418 Elverum, Norway
2) Division of Epidemiology, Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, 0403 Oslo, Norway
3) Norwegian Centre for Addiction Research, University of Oslo, Norway

Correspondence: Ingeborg Hartz, e-mail: ingeborg.hartz@hihm.no

ABSTRACT

Objectives: The Norwegian Government urges that actions are needed to stimulate the working capacity in disability pensioners (DPs) with such a potential. Information on factors that may impair rehabilitation efforts, including use of potentially addictive drugs, may be useful in this context. Thus, the aim was to study the association between DP on initiation as well as long-term use of benzodiazepines (BZDs), and to describe aspects of problematic use of BZDs in terms of: long-term use pattern, including escalation of dose over time, and use of other potentially addictive drugs.

Methods: We followed a cohort of 8,942 men and 10,578 women aged 40, 45, 60 years (non-users of BZDs at baseline), who participated in health surveys in 2000-01 in three Norwegian counties, with respect to use of BZDs, and other potentially addictive drugs, by linkage to the Norwegian Prescription Database (NorPD) for 2004-2007. Information on DP status was retrieved from Statistics Norway.

Results: Incident BZD use was highest among female DPs; 18-20% compared to 5-8% of the non-DPs. Multivariable analyses revealed an independent effect of DP on incident (OR 1.6 (95% CI 1.4-2.0)) and long-term use (OR 2.47 (95% CI 1.90-3.20)) of BZDs. Among incident users, 51-60% of the DPs retrieved BZDs throughout the period 2004-07, as compared to 32-33% of the non-DPs. The annual median defined daily doses (DDDs) of BZDs among long-term users increased throughout the period 2004-07, most pronounced in the youngest DPs; from 50 (interquartile range (IQR) 14,140) DDD to 205 (IQR 25,352) DDD.

Conclusions: The chance of being prescribed BZDs as well as becoming a long-term user was higher among DPs. High continuation rates, with a steadily increasing annual amount of use among the long-term users may reflect an unfavourable use pattern of potentially addictive drugs among DPs, most worrisome among the youngest.

INTRODUCTION

Socioeconomic inequalities of health have become an important part of the political agenda in Norway and other countries[1]. Commonly used measures of socioeconomic status are level of education, occupation and level of income[2]. In addition; other measures of sosioeconomic status are used, such as disability pension which is associated with a lower educational level[3]. Equal access to and quality of health care is supposed to be a fundamental part of the Norwegian welfare-system[1]. In this context; drugs should be prescribed according to medical need, irrespective of socioeconomic circumstances, and problematic use of potentially addictive drugs should be equally avoided.

Studies on socioeconomic inequalities in drug use are relatively scarce in the literature. One area highlighted, however, concerns socioeconomic inequalities in the use of statins. Statins have a well documented beneficial effect on cardiovascular morbidity and mortality[4]. Thus, an inequality in statin use, due to sosioeconomic factors and not need, would imply inquality in the prevention of one of the leading causes of death in Norway. Swedish and Danish cross-sectional studies have shown a socioeconomic gradient in use of statins[5-7]. However, a recent Norwegian study showed that this gradient could be explained by different cardiovascular disease (CVD) risk factor profiles (medical need) prior to the initiation of therapy, at least for primary CVD prevention[8]. In the secondary prevention group, however, there was a tendency to a higher statin use among the highly educated compared with people of lower educational level, after adjustment for other CVD risk factors, particularly in women. It may reflect that highly educated women may be more aware of their own health and new treatments than women of low educational level, which in turn may add up as a factor contributing to the observed social gradient in cardiovascular mortality.

The proportion of Norwegians on disability pensions has doubled since the 1980s[9]. About 11 per cent of the working population (18-67 years) now receives disability benefit in Norway which constitutes both social and economical challenges. The Norwegian Government has urged action to arrest the upward trend of people on disability pension. Information on factors that may impair rehabilitation efforts, including unfavourable use of potentially addictive drugs, may be useful in this context.

In Norway, and other OECD countries, mental

health disorders and musculoskeletal problems are the main reasons for claiming disability benefit[9]. Benzodiazepines (BZDs) have anxiolytic, sedative, anticonvulsant and muscle-relaxant effects, so they are likely to be used by disability pensioners to deal with these problems[10]. However, there are concerns about benzodiazepines because of their potential adverse effects, which include impaired cognitive function and psychomotor skills, unwanted sedation, as well as dependence associated with long-term use[10,11]. Because of this, benzodiazepines are only recommended for short-term use over a few weeks[12], and guidelines emphasize that combined use with other potentially addictive drugs, such as opioids and carisoprodol, is especially problematic[13]. Unfavorable use may be of particular concern in disability pensioners, as it may add yet another potential problem to the deterioration of people's daily functioning.

To our knowledge, information on the use of potentially addictive drugs according to disability pension status is scarce in the literature. However, recent studies evaluating use of potentially addictive drugs over a 20 year period (from 40 to 60 years of age), suggest that such drugs are extensively used among disability pensioners, and that disability pension was an independent predictor of initiation as well as continued use of BZDs[14,15].

These studies had a special focus on long-term use, with a 20 year period between the two measuring points. Thus, a limitation of these studies, was 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 the previous study[9]. 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 presented will be underestimated, and biased towards the null.

Also, information on long-term use was collected in a limited cohort of individuals, 40-42 year olds only. We do not know whether these findings are valid for other age-groups. And last, the study population constituted individuals living in regions in Norway with above average consumption of anxiolytics and hypnotics over the past years, compared to other Norwegian regions[16]. Thus the trends shown in the previous studies may not be representative to other parts of Norway.

In this current study, we wanted to extend the knowledge of aspects of use of potentially addictive drugs to other age-groups, based on more recent data from regions with average overall consumption of these drugs. The aims of our study were to evaluate disability pension as a predictor of initiation and long-term use of benzodiazepine use among individuals reporting to be non-users at baseline, adjusting for several other factors that may influence use of such drugs. Further, other aspects of problematic use of benzodiazepines studied were: long-term use pattern in terms of percentage of incident users becoming long-term users and escalation of dose over time, and prevalence of medication with other potentially addictive drugs (z-hypnotics, opioids and carisoprodol).

MATERIALS AND METHODS

Health surveys – information on independent variables

Data from Cohort of Norway (CONOR) was included in this study, which is a collection of health data and blood samples from several Norwegian health surveys described elsewhere[17,18]. CONOR data from population based surveys conducted in 2000-01 in the three Norwegian counties Oslo (HUBRO and the Oslo II study), Hedmark and Oppland (The OPPHED study) are included in this study, which cover both rural and urban regions. Our analyses are restricted to data on participants aged 61 years and younger, thus including people below the early age of retirement (contractual pension) only. At the time of investigation, the subjects were aged 40-41, 45-47 and 59-61 years (from now on referred to as two age-groups: 40+45 and 60). All subjects in selected age cohorts were invited to participate in the respective surveys. In these age cohorts 18,612 men and 18,273 women were invited in the HUBRO and OPPHED study. Of these, 9,363 men (50.3%) and 11,236 women (61.5%) participated and agreed to the storage of blood samples and data for research purposes and agreed to have their data linked to other health registers (Figure 1). In addition, our study-population included 46 male participants aged 61 years from the Oslo II health study, in which the overall response rate was 48.7%[17]. 129 men and 124 women who died or emigrated before January 1 2004 were excluded from analyses. In a second step we removed all those whose drugs were reimbursed for treatment of cancer (Figure 1).

As our purpose was to study incident use of BZDs, BZD users at baseline were excluded. The drug use questions included an open question on drug trade names. Those who wrote trade names of benzodiazepines, were excluded from our study (245 men and 442 women). And last, persons with missing information in the administrative register on disability pension status (14 men and 6 women) were excluded resulting in a study-population of 19,520 people (8,942 men and 10,578 women).

The participants completed a self-administered questionnaire covering drug use questions, history of diseases and risk factors, and different lifestyle habits such as alcohol use, smoking and physical activity and others. See Table 1 for details on questions and variable definition. The English version of the questionnaire, as well as further details of the surveys, is available at the home page of the Norwegian Institute of Public Health[18].

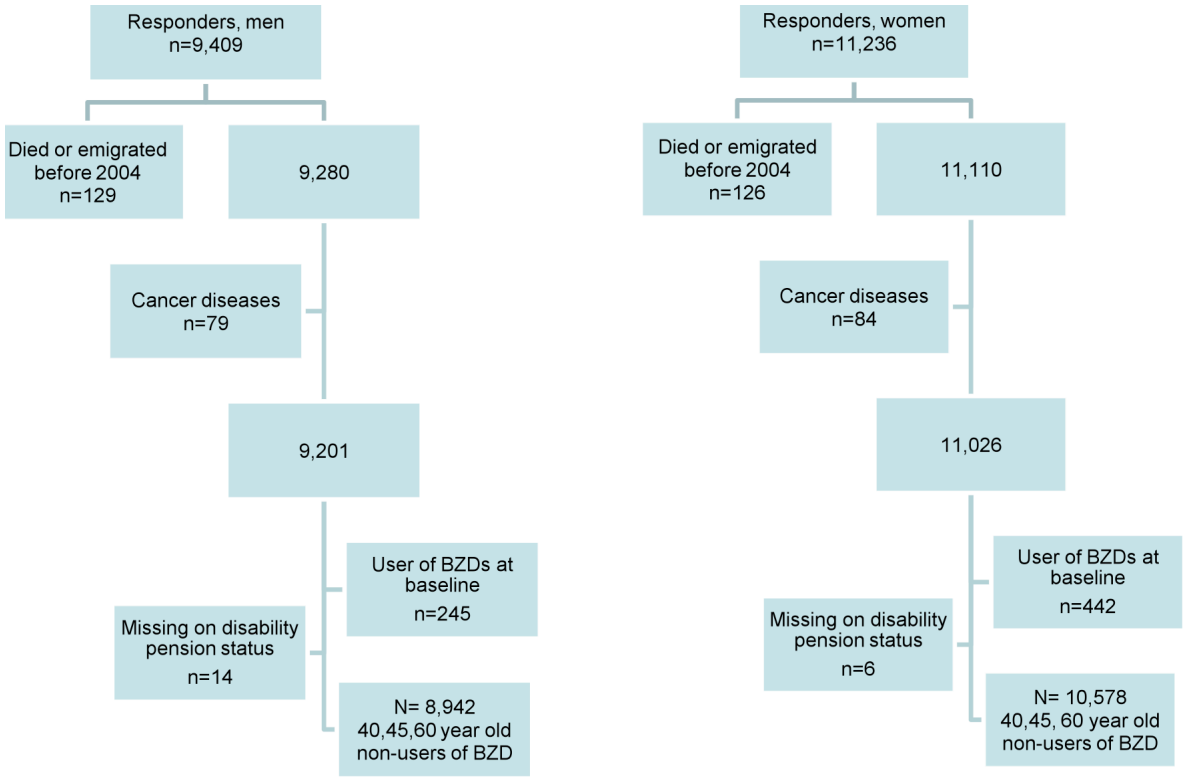


Figure 1. Flow chart for the study population. Health surveys in Oslo, Hedmark and Oppland 2000-2001. BZD = benzodiazepine.

Table 1. Questions with answering categories and variable definition from the health surveys in Oslo, Oppland and Hedmark 2000-2001.

Self-administered questionnaire	Answering alternatives	Variable definition
Alcohol consumption habits		
Approximately how often during the past 12 months have you consumed alcohol?	Teetotaller (1); not during the last year (2); a few times the last year (3); once per month (4); 2-3 times per month (5) about once a week (6) 2-3 times per week (7) 4-7 times per week (8)	Teetotallers/seldom =1-3; once a week-once a month =4-6; several times a week =7,8
Smoking habits		
Did you / do you smoke daily at present?	Yes (1) previously (2) no (3)	smokers =1; ex-smokers= 2; non-smokers =3
Physical activity		
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
Self-perceived health		
What is your current health status ?	poor (1); not so good (2); good (3); very good (4)	Self-perceived health not good=1,2
Mental health problems		
Do you have or have you ever had psychological problems for which you have sought help?	Yes (1)/no (2)	mental health problems =1; no=2
Fibromyalgia/chronic pain syndrome		
Do you have or have you ever had fibromyalgia/chronic pain syndrome ?	Yes (1)/no (2)	fibromyalgia/chronic pain syndrome =1; no=2
Cardiovascular history		
Do you have or have you ever had heart attack, angina pectoris (heart cramp), cerebral stroke/ brain hemorrhage	Yes (1) no (2) on each question	CVD history =1 on either question, otherwise no CVD history

Information on disability pension status

The variable "current activity status" from the nationwide population and housing census in Norway 2001 (Statistics Norway) was used to categorize individuals according to disability pension status[19]. This variable is based on information from several administrative registers, and contains information on all citizens living in Norway. The variable categorizes Norwegian individuals according to their labour force participation; employed, unemployed, in education, or receipt of national insurance benefit (disability-, retirement- or survivor pension). The study population was categorized as either receivers or non-receivers of a disability pension.

Norwegian Prescription Database (NorPD) – information on dependent variables

Prescription data about benzodiazepines in 2004-2007 were drawn from the Norwegian Prescription Database (NorPD) which covers the entire nation (4.7 million inhabitants)[20,21]. 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 living outside institutions 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[22]. 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)). The code of reimbursement is also recorded and this may function as a proxy of diagnosis. Code §9.9 is dedicated to cancer diseases.

Benzodiazepines were defined by the ATC-codes N05BA (anxiolytics), N05CD (hypnotics) and N03AE01 (clonazepam), benzodiazepine-like drugs (z-hypnotics; zolpidem and zopiclone) by the ATC-code N05CF, opioids by the ATC-code N02A and carisoprodol by the ATC-code M01BA02. Incident use was defined when an individual (non-user at baseline) was dispensed at least one prescription of a benzodiazepine during the period 1 January 2004 – 31 December 2004. Long-term use was defined when an individual (non-user at baseline) was dispensed at least one prescription of a benzodiazepine each of the years 2004 to 2007. Among BZD users in 2004, the proportion of long-term users throughout the period 2004-07 was calculated, according to disability pension status and age.

In addition, among the long-term benzodiazepine users, the annual amount of BZDs dispensed in the period 2004-2007 was calculated in terms of total defined daily doses (DDDs).

A DDD in clinical practice is defined as the assumed average maintenance dose per day for a drug used on its main indication in adults[23]. The DDDs for the benzodiazepines registered in Norway, and included in our analysis, are as follows; diazepam 10 mg, oxazepam 50 mg, alprazolam 1 mg, nitrazepam 5 mg, flunitrazepam 1 mg, midazolam 15 mg, clonazepam 8 mg. Data from the health surveys, administrative register and NorPD were linked based on the unique encrypted identification number.

Statistics

Chi-square test was used to assess equality of proportions across the groups of drug use. Mann-Whitney test was used for variables with a skewed distribution (DDDs, presented as median and interquartile ranges (IQR)). Association between disability pension status and others factors with incident BZD use in 2004 and long-term BZD use (2004-07) was estimated by logistic regression, and presented as crude and adjusted odds ratios (ORs) with 95% confidence intervals (CI). All analyses were done using SPSS 17.0 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.

RESULTS

Baseline characteristics (non-users of benzodiazepines)

Characteristics of the study population, non-users of benzodiazepines at baseline, are shown in Table 2. There was a higher prevalence of teetotallers and current daily smokers among disability pensioners. Further, there was a higher proportion of unmarried people (except in 60 year old women) and physically inactive persons (except in 60 year old men) among receivers of a disability pension.

About 2/3 of the disability pensioners reported poor self-perceived health at baseline, irrespective of age and gender. Also, the prevalences of mental health problems, fibromyalgia/chronic pain syndrome and cardiovascular disease were significantly higher among receivers of a disability pension.

Self-reported use of z-hypnotics, opioids and carisoprodol at baseline were higher among disability pensioners, except for z-hypnotics in 60-year old men.

Retrieval of prescription drugs in 2004 and 2004-2007

In both genders, and irrespective of age, incident BZD use 3-4 years later was significantly higher among disability pensioners (Table 2). Highest initiation rates were observed among female disability pensioners, of whom 18-20% had started BZDs, as compared to 5-8% of the female non-receivers of a disability pension at baseline.

Table 2. Prevalence (n (%)) of baseline characteristics among men and women who were nonusers of benzodiazepines when surveyed in 2000-01. Use of prescription drugs retrieved from the Norwegian Prescription Database in 2004-2007 according to baseline characteristics.

	40+45 years						60 years					
	Men			Women			Men			Women		
	Disability pension (2001)			Disability pension (2001)			Disability pension (2001)			Disability pension (2001)		
	Yes (N=167)	No (N=5735)	p	Yes (N=268)	No (N=7059)	p	Yes (N=483)	No (N=2557)	p	Yes (N=674)	No (N=2577)	p
Baseline characteristics 2000-01												
Unmarried	107 (65.2)	2226 (38.8)	<0.000	156 (58.2)	2725 (38.6)	<0.000	188 (38.9)	701 (27.4)	<0.000	255 (37.8)	919 (35.7)	0.296
Alcohol habits												
Teetotallers/seldom	66 (41.3)	1037 (18.3)		142 (54.0)	1718 (24.6)		156 (33.3)	451 (17.8)		323 (48.5)	746 (29.3)	
Once a week-once a month	71 (44.4)	3202 (56.4)		92 (35.0)	3927 (56.2)		216 (46.1)	1170 (46.1)		255 (38.3)	1197 (46.9)	
Several times a week	23 (14.4)	1435 (23.3)	<0.000	29 (11.0)	1341 (19.2)	<0.000	97 (20.7)	918 (36.2)	<0.000	88 (13.2)	607 (23.8)	<0.000
Smoking habits												
Current daily smokers	87 (52.1)	1755 (30.6)		129 (48.1)	2323 (32.9)		188 (38.9)	584 (22.8)		221 (32.8)	531 (20.6)	
Exsmokers	30 (18.0)	1474 (25.7)		53 (19.8)	1856 (26.3)		174 (36.0)	1040 (40.7)		177 (26.3)	699 (27.1)	
Non smokers	50 (29.9)	2506 (43.7)	<0.000	86 (32.1)	2880 (40.8)	<0.000	121 (25.1)	933 (36.5)	<0.000	276 (40.9)	1347 (52.3)	<0.000
Seldom/never physical active	61 (39.4)	1392 (25.1)	<0.000	79 (31.7)	1332 (19.5)	<0.000	102 (22.6)	484 (19.4)	0.123	195 (29.8)	522 (21.0)	<0.000
Self-perceived health (not good)	117 (72.7)	966 (17.0)	<0.000	180 (68.7)	1310 (18.8)	<0.000	315 (66.2)	556 (22.0)	<0.000	448 (67.2)	698 (27.5)	<0.000
Mental health problems[a]	74 (44.3)	587 (10.2)	<0.000	119 (44.4)	1157 (16.4)	<0.000	109 (22.6)	212 (8.3)	<0.000	175 (26.0)	322 (12.5)	<0.000
Fibromyalgia/chronic pain syndrome	27 (16.2)	150 (2.6)	<0.000	91 (34.7)	472 (6.7)	<0.000	53 (11.0)	65 (2.5)	<0.000	255 (37.8)	265 (10.3)	<0.000
Cardiovascular history	17 (10.2)	110 (1.9)	<0.000	11 (4.1)	46 (0.7)	<0.000	134 (27.7)	249 (9.7)	<0.000	79 (11.7)	95 (3.7)	<0.000
Drug use at baseline (selfreport)												
z-hypnotics	5 (3.0)	65 (1.1)	0.029	21 (7.8)	139 (2.0)	<0.000	7 (1.4)	40 (1.6)	0.851	52 (7.7)	102 (4.0)	<0.000
opioids	25 (15.0)	177 (3.1)	<0.000	47 (17.5)	277 (3.9)	<0.000	51 (10.6)	65 (2.5)	<0.000	78 (11.6)	101 (3.9)	<0.000
carisoprodol	6 (3.6)	28 (0.5)	<0.000	14 (5.2)	78 (1.1)	<0.000	7 (1.4)	6 (0.2)	0.002	19 (2.8)	16 (0.6)	<0.000
NorPD 2004[b]												
benzodiazepines	22 (13.2)	173 (3.0)	<0.000	53 (19.8)	384 (5.4)	<0.000	53 (11.0)	109 (4.3)	<0.000	121 (18.0)	214 (8.3)	<0.000
DDD (IQR) among users	73 (25,196)	20 (10,65)	<0.000	40 (14,116)	15 (9,38)	<0.000	50 (18,178)	20 (10,50)	<0.000	50 (20,150)	18 (10,50)	<0.000
z-hypnotics	18 (10.8)	243 (4.2)	<0.000	55 (20.5)	508 (7.2)	<0.000	49 (10.1)	184 (7.2)	0.025	138 (20.5)	346 (13.4)	<0.000
opioids	35 (21.0)	537 (9.4)	<0.000	71 (26.5)	712 (10.1)	<0.000	89 (18.4)	286 (11.2)	<0.000	164 (24.3)	320 (12.4)	<0.000
carisoprodol	10 (6.0)	135 (2.4)	0.009	30 (11.2)	276 (3.9)	<0.000	15 (3.1)	34 (1.3)	0.004	41 (6.1)	63 (2.4)	<0.000
NorPD 2004-07[c]												
benzodiazepines	9 (5.4)	59 (1.0)	<0.000	29 (10.8)	117 (1.7)	<0.000	29 (6.0)	32 (1.3)	<0.000	76 (11.3)	74 (2.9)	<0.000

*p-value<0.05; **p-value<0.01; ***p-value<0.001; n.s., not significant

[a] Sought help for mental health problems

[b] use was defined as retrieveal of at least 1 prescription in 2004

[c] long-term use was defined as retrieveal of at least 1 prescription in 2004, 2005, 2006 and 2007

Prevalence of use of all other potentially addictive substances, such as z-hypnotics, opioids and carisoprodol had increased 3-4 years later, irrespective of age, gender and disability pension status at baseline. E.g. in 2004, 18-27% of disability pensioners retrieved a prescription on an opiod, about twice the level of retrieval among the non-receivers of a disability pension.

A significantly higher proportion of the disability pensioners became long-term users of benzodiazepines as compared to the non-receivers of a disability pension, 5-6% of the male and 10-11% of the female disability pensioners.

Predictors of BZD use

Univariate and adjusted ORs for incident retrieval of benzodiazepine prescription were higher among disability pensioners, as compared with those registered as non-receivers of a disability pension 3-4 years in the past (Table 3).

Further, univariate OR for long-term use of benzodiazepines was above six times higher among the receivers compared to the non-receivers of a disability pensioners (Table 3). After adjustment for age, sex, lifestyle, physical and mental health, and socio-economic variables the OR was lowered to 2.5 (1.9-3.2). Other independent predictors of long-term BZD use were; increasing age, female gender, an unmarried status, previous smoking, physical inactivity, poor self-perceived health, fibromyalgia/chronic pain syndrome and a CVD history. The strongest predictor of long-term BZD use was self-reported mental health problems at baseline.

Patterns of long-term BZD use, and amount of use among the long-term BZD users

The proportion of incident BZD users in 2004 who continued to retrieve BZD prescriptions throughout the period 2004-07 was higher among receivers compared to the non-receivers of a disability pension at baseline (Figure 2). Among BZD users in 2004, half of the

Table 3. Number (n) and proportion (%) of incident (2004) and long-term (2004-07) BZD use among participants in population based studies 2000-2001, non-users of BZD at baseline (8,942 men and 10,578 women). Association between disability pension status and others factors with incident (2004) and long-term (2004-07) BZD use; unadjusted and adjusted odds ratio (OR) with 95% confidence interval (CI).

		Incident BZD 2004 In the model			Long-term BZD user (2004-07) In the model	
	n (%)	Unajusted OR (95%CI)	Adjusted* OR (95%CI)	n (%)	Unajusted OR (95%CI)	Adjusted* OR (95%CI)
Disability pension						
No	880 (4.9)	1.0 (referent)	1.0 (referent)	282 (1.6)	1.0 (referent)	1.0 (referent)
Yes	249 (15.6)	3.59 (3.01-4.18)	1.64 (1.36-1.97)	143 (9.0)	6.18(5.02-7.61)	2.47 (1.90-3.20)
Age						
40+45	632 (4.8)	1.0 (referent)	1.0 (referent)	214 (1.6)	1.0 (referent)	1.0 (referent)
60	498 (7.9)	1.71 (1.52-1.94)	1.56 (1.36-1.79)	211 (3.4)	2.11 (1.74-2.56)	1.72 (1.37-2.15)
Sex						
Men	358 (4.0)	1.0 (referent)	1.0 (referent)	129 (1.4)	1.0 (referent)	1.0 (referent)
Women	772 (7.3)	1.89 (1.66-2.15)	1.82 (1.58-2.10)	296 (2.8)	1.97 (1.60-2.43)	1.81 (1.44-2.27)
Unmarried						
No	601 (4.9)	1.0 (referent)	1.0 (referent)	202 (1.6)	1.0 (referent)	1.0 (referent)
Yes	527 (7.2)	1.51 (1.34-1.71)	1.20 (1.05-1.36)	223 (3.1)	1.88 (1.55-2.83)	1.39 (1.13-1.72)
Alcohol						
Teetotallers/seldom	316 (6.8)	1.0 (referent)	1.0 (referent)	118 (2.5)	1.0 (referent)	1.0 (referent)
Once a week-once a month	547 (5.4)	0.81 (0.68-0.96)	1.07 (0.89-1.29)	205 (2.0)	0.87 (0.62-1.08)	1.17 (0.87-1.58)
Several times a week	253 (5.6)	0.78 (0.68-0.90)	1.04 (0.89-1.21)	95 (2.1)	0.79 (0.63-1.00)	1.18 (0.92-1.51)
Smoking						
Non-smokers	362 (4.4)	1.0 (referent)	1.0 (referent)	116 (1.4)	1.0 (referent)	1.0 (referent)
Exsmokers	295 (5.4)	1.91 (1.66-2.21)	1.73 (1.49-2.02)	105 (1.9)	2.53 (2.01-3.19)	2.16 (1.68-2.78)
Current daily smokers	473 (8.1)	1.23 (1.05-1.44)	1.18 (1.00-1.40)	204 (3.5)	1.36 (1.04-1.77)	1.33 (1.00-1.76)
Seldom/never physical active						
No	777 (5.3)	1.0 (referent)	1.0 (referent)	277 (1.9)	1.0 (referent)	1.0 (referent)
Yes	313 (7.5)	1.45 (1.27-1.67)	1.29 (1.12-1.49)	132 (3.2)	1.70 (1.38-2.10)	1.41 (1.13-1.76)
Self-perceived health (not good)						
No	631 (4.3)	1.0 (referent)	1.0 (referent)	196 (1.3)	1.0 (referent)	1.0 (referent)
Yes	487 (10.6)	2.65 (2.34-2.99)	1.57 (1.36-1.82)	224 (4.9)	3.79 (3.12-4.61)	1.78 (1.41-2.43)
Mental health problems						
No	731 (4.4)	1.0 (referent)	1.0 (referent)	245 (1.5)	1.0 (referent)	1.0 (referent)
Yes	399 (14.5)	3.71 (3.26-4.22)	2.85 (2.47-3.28)	179 (6.5)	4.66 (3.83)	3.21 (2.58-9.98)
Fibromyalgia/chronic pain syndrome						
No	944 (5.2)	1.0 (referent)	1.0 (referent)	336 (1.9)	1.0 (referent)	1.0 (referent)
Yes	186 (13.4)	2.83 (2.39-3.45)	1.31 (1.08-1.60)	89 (6.4)	3.65 (2.87-4.64)	1.31 (0.98-1.74)
Cardiovascular disease history						
No	1050 (5.6)	1.0 (referent)	1.0 (referent)	387 (2.1)	1.0 (referent)	1.0 (referent)
Yes	80 (10.8)	2.04 (1.60-2.59)	1.47 (1.13-1.93)	38 (5.1)	2.56 (1.87-3.60)	1.54 (1.05-2.25)

*Adjusted for all variables in Table

youngest (40+45 years at baseline) and 60% of the oldest (60 years at baseline) continued to retrieve benzodiazepines throughout the period 2004-07, as compared to a third of the non-receivers of a disability pension (Figure 2).

Among long-term users, the median amount of BZDs retrieved among disability pensioners in 2004 was 50 DDD, as compared to 18-20 DDD among the non-receivers of a disability pension (Figure 3). The annual median DDD of benzodiazepines among continued users increased steadily throughout the period, most pronounced among the youngest disability pensioners.

DISCUSSION

In a study-population reporting to be non-users of BZDs at baseline; the proportion of disability pensioners that had started benzodiazepines 3-4 years later were about fourfold among 40+45 year old and about doubled in the 60 year old compared to those registered as non-receivers of a disability pension at baseline. Further, once started BZD use in 2004, continuation rates were high, with a steadily increasing amount of BZDs (DDDs) throughout the period 2004-2007.

A higher use of benzodiazepine use among those registered as disability pensioners may partly be explai-

Figure 2. Proportion of long-term use of benzodiazepines among users (men and women) in 2004, throughout the period 2004-07, according to disability pension status and age. DP = disability pensioners.

DP-status (age)	2004 n (%)	2005 n (%)	2006 n (%)	2007 n (%)
+ DP (40+45)	75 (100)	56 (74.7)	46 (61.3)	38 (50.7)
– DP (40+45)	557 (100)	292 (52.4)	221 (39.7)	176 (31.6)
+ DP (60)	174 (100)	138 (79.3)	119 (68.3)	105 (60.3)
– DP (60)	323 (100)	170 (52.6)	135 (41.8)	106 (32.8)

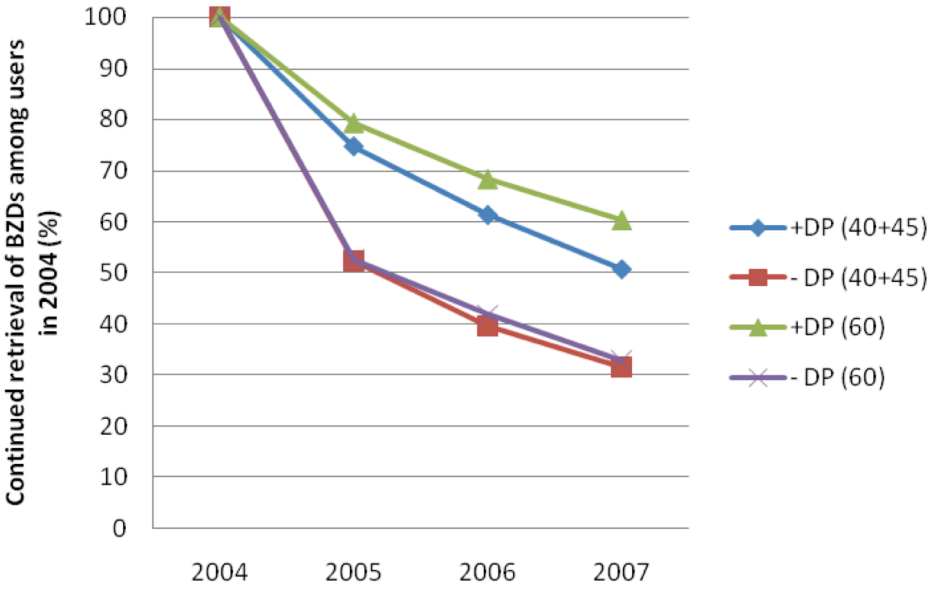
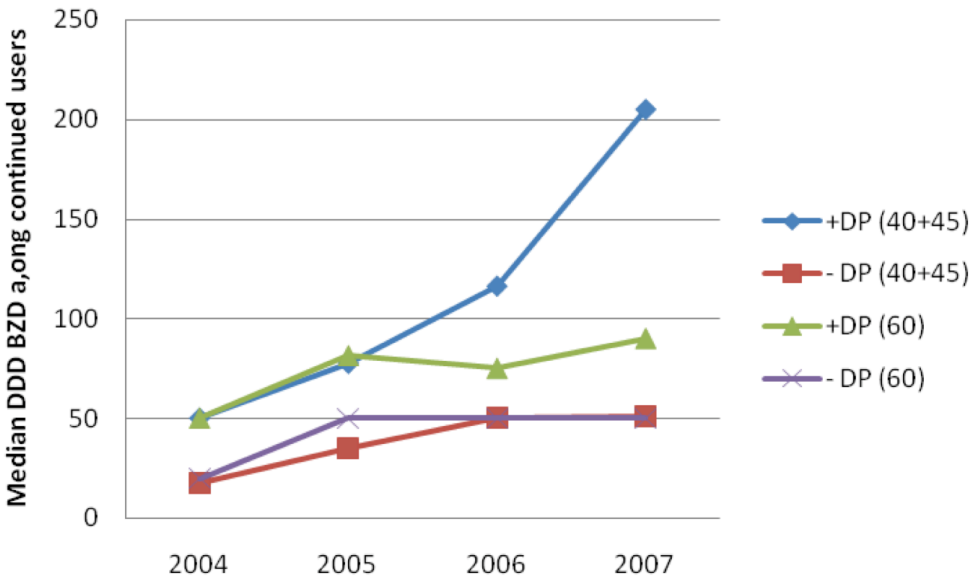


Figure 3. Median amount (DDDs with interquartile range (IQR)) of benzodiazepines retrieved among long-term users (men and women) throughout the period 2004-2007, according to age and disability pension status. DP= disability pensioners.

DP status (age)	2004 DDD (IQR)	2005 DDD (IQR)	2006 DDD (IQR)	2007 DDD (IQR)
+ DP (40+45)	50 (15,140)	78 (29, 220)	116 (49, 116)	205 (25, 352)
– DP (40+45)	18 (10,50)	35 (13, 100)	50 (20, 120)	51 (21, 150)
+ DP (60)	50 (20,150)	81 (29, 200)	75 (30, 170)	90 (48, 200)
– DP (60)	20 (10,50)	50 (15, 100)	50 (20, 125)	50 (25, 150)



ned by a higher prevalence of mental health symptoms in this group at baseline. Mental health problems are the main reason for being granted a disability pension in Norway, in young people in particular[24]. Thus, mental health problems were the strongest predictor of incident and long-term BZD use, and almost half of all 40+45 year old disability pensioners in our study were registered as receivers of a disability pension. Still, however, adjustment for various confounders, including self-perceived health and self-reported presence of mental health problems at baseline, revealed an independent effect of disability pension on the initiation and thereby long-term use of benzodiazepines 3-4 years later. Our study supports that initiation and long-term use of BZDs may be attributed to the DP situation which itself may bring about a number of psychological problems as a result of exclusion from the social and personal advantages associated with being a part of the workforce[25]. Drug treatment with benzodiazepines may be initiated to relieve these symptoms. Our evaluation of disability pension as a risk-factor of benzodiazepine use must, however, be interpreted with caution. Even if many potential confounders associated with prescription of benzodiazepines were registered and adjusted for in our analysis, all possible confounders may not have been taken into account. Our observations of an independent effect of disability pension on the initiation and long-term use of BZDs, however, are in agreement with a previous study evaluating incident benzodiazepine-taking behaviour over a 20 year span[14,15].

Because of concerns related to the potential side-effects, such as impaired cognitive function and psychomotor skills, and addiction problems[10,11], benzodiazepines are only recommended for short-term use over a few weeks[12]. Still 50-60 per cent of those disability pensioners who retrieved a BZD prescription in 2004 continued to retrieve BZD prescriptions throughout the period 2004-2007. Parallel continuation rates were observed over a 20-year period in a previous study; more than half of those on disability pensions continued to receive benzodiazepine prescriptions 20 years later, a span covering a large part of the potential active workforce period[14]. Our findings add to observations in other studies on long-term use; having once entered a cohort of benzodiazepine users, the probability of still being part of that cohort in the following years is consistently high in different populations[26-28]. Thus, in this context, high initiation rates among the youngest disability pensioners observed in our study may perhaps be most worrisome. Once started, larger proportions will most likely continue to use BZDs throughout their potential work-force period.

One could argue that one annual prescription over a 4 year period is neither an outcome for long-term use, nor an addictive use pattern. However, the observed annual increase in amount of benzodiazepines dispensed over this 4-year period indicates more than sporadic use, among the youngest disability pensioners (40+45 years) in particular. In 2004 half of the youngest disability pensioners were dispensed an annual amount of benzodiazepines corresponding to the use of a daily dose every week (median 50 daily doses), increasing to retrieval of a daily dose every second day in 2007 (median 205 daily doses). A corresponding amount, a dose every second day, was observed in the previous study evaluating continued use of benzodiazepines over a 20-year period[14]. In addition, and relevant to the discussion of unfavourable use of potentially addictive drugs, baseline level (2000-2001) of use of all other potentially addictive substances, such as z-hypnotics, opioids and carisoprodol had increased 3-4 years later in disability pensioners, irrespective of age and gender. Parallel, as revealed in our previous study, the majority of those who were still dispensed benzodiazepines 20 years later, were also dispensed opioids; half of all men and 3 out of four women. 15-20% retrieved benzodiazepines combined with both opioids and carisoprodol[14]. Guidelines emphasize that combined use with other potentially addictive drugs, such as opioids and carisoprodol, is especially problematic[12,13]. These recommendations are being violated when continued and combined use of benzodiazepines exists to the extent observed in our present and previous studies. Unfavourable use may be of particular concern in disability pensioners, as it may add yet another potential problem to the deterioration of people's daily functioning, help consolidate the disability situation.

As in previous studies, in the present study we chose to focus on use of traditional benzodiazepines, with its well known potential of causing addiction problems and other negative effects interfering with people's daily functioning[10,11]. Thus, we excluded prescriptions on benzodiazepine-like hypnotics from our analysis. In Norway benzodiazepine-like hypnotics, z-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, 85-90% of all individuals who retrieved at least one prescription on a hypnotic in Oslo, Hedmark and Oppland were users of benzodiazepine-like hypnotics in 2007[21]. Recent literature, however, adds to the growing evidence that these substances have a similar potential for negative effects as traditional benzodiazepines[29-31]. Still we wanted to restrict our analysis to the prescription of the traditional benzodiazepines, which constitutes a better documented marker of an addictive use pattern[29,32,33].

This study is prospective with information from nationwide registers on exposure (disability pension status) and outcome (BZDs) variables. However, our study-population is attendants in health surveys, in which attendance rates at 50-60% may imply a risk of selection bias. Unfortunately we do not have information on all non-attendants in our study. However, an evaluation of the non-attendees in the Oslo Health Survey (HUBRO) was performed; receivers of a dis-

ability pension were over-represented among the non-attendees, while some health indicators, including mental health (HSCL), probably did not differ[34]. Low attendance may bias the representativity of baseline characteristics or prevalences, but is less likely to influence estimates of associations such as odds ratios. Further, self-reported use of BZD at baseline may be underreported. In general, anxiolytics and hypnotics/sedatives are prone to be underreported, possibly due to the stigma of mental health problems[35]. Thus, there may be an unknown number of BZD users at baseline included in our study-population.

In conclusion, compared to previous studies which had a special focus on incident and long-term use of benzodiazepines over a 20-year period, this study adds complementary and new information of aspects of use of potentially addictive drugs among disability pensioners in Norway. Our study suggests that BZDs, and other potentially addictive drugs, are extensively used among disability pensioners, and that disability pension may have an independent effect on initiation followed by long-term use of BZDs. Once started, rates of continued retrieval of BZDs are high, with a steadily increasing annual amount of use, most pronounced among the youngest disability pensioners. Efforts to bring those with potential to work back into employment have been a part of the political agenda for the last decade. Improved management of BZD use may be one part of this effort.

ACKNOWLEDGEMENT

The data collection was conducted as a part of the Health survey in Oslo, Hedmark and Oppland in 2000-01, performed by the National Health Screening Service of Norway (now Norwegian Institute of Public Health). This paper is a part of the project "The epidemiology of prescription drug use. A record-linkage study in Norway", which is financially supported by The Norwegian Research Council. No other external financial support for the present work was received. Commercial interest holders have not employed the authors otherwise and no conflicts of interest were present.

REFERENCES

1. Det kongelige helse- og omsorgsdepartement. St. mld .nr. 20 (2006-2007). Nasjonal strategi for å utjevne sosi–ale helseforskjeller (http: //www.regjeringen.no/pages/1936477/PDFS/STM200620070020000DDDPDFS.pdf).
2. Næss Ø, Rognerud M, Strand B. Sosial ulikhet i helse – en faktarapport. Rapport 2007: 1, Nasjonalt folkehelseinstitutt.
3. Krokstad S, Westin S. Disability in society – medical and non-medical determinants for disability pension in a Norwegian total county population study. *Soc Sci Med* 2004; **58**: 1837-48.
4. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; **360**: 7-22.
5. Weitoft GR, Rosen M, Ericsson O, Ljung R. Education and drug use in Sweden – a nationwide register-based study. *Pharmacoepidemiol Drug Saf* 2008; **17**: 1020-8.
6. Mortensen JT, Olesen AV, Boggild H, Olsen J, Westergard-Nielsen NC. Socioeconomic correlates of drug use based on prescription data: a population-based cross-sectional register study in Denmark 1999. *Dan Med Bull* 2007; **54**: 62-6.
7. Thomsen RW, Johnsen SP, Olesen AV, Mortensen JT, Boggild H, Olsen J, et al. Socioeconomic gradient in use of statins among Danish patients: population-based cross-sectional study. *Br J Clin Pharmacol* 2005; **60**: 534-42.
8. Selmer R, Sakshaug S, Skurtveit S, Furu K, Tverdal A. Statin treatment in a cohort of 20 212 men and women in Norway according to cardiovascular risk factors and level of education. *Br J Clin Pharmacol* 2009; **67**: 355-62.
9. Norges offenlige utredninger (NOU) 2007: 4. Ny uførestønad og ny alderspensjon til uføre. Avgitt til arbeids- og inkluderingsdepartementet. (http://www.regjeringen.no/nb/dep/aid/dok/NOUer/2007/NOU-2007-4.html?id=467193)
10. O'Brien CP. Benzodiazepine use, abuse, and dependence. *J Clin Psychiatry* 2005; **66** Suppl 2: 28-33.
11. Barker MJ, Greenwood KM, Jackson M, Crowe SF. Cognitive effects of long-term benzodiazepine use: a meta-analysis. *CNS Drugs* 2004; **18**: 37-48.
12. Vanedannende legemidler. Forskrivning og forsvarlighet. IK-2755. Oslo: Helsetilsynet, 2001. (www.helsetilsynet.no/upload/Publikasjoner/andrepublikasjoner/vanedannende_legemidler_forskrivning_forsvarlighet_ik-2755.pdf).
13. Terapianbefaling: Bruk av opioider ved behandling av langvarige, non-maligne smertetilstander – en oppdatering (2008). Norsk legemiddelverk (Norwegian Medicines Agency), Oslo, Norway (http://www.legemiddelverket.no/templates/InterPage____69246.aspx).
14. Hartz I, Tverdal A, Skurtveit S. Disability pension as predictor of continued use of benzodiazepines. *Pharmacoepidemiol Drug Saf* 2009; **18**: S93.

15. Hartz I, Lundesgaard E, Tverdal A, Skurtveit S. Disability pension is associated with the use of benzodiazepines 20 years later: A prospective study. *Scand J Public Health* 2009; **37**: 320-6.
16. Drug consumption in Norway. The Norwegian Institute of Public Health. (http://www.fhi.no/eway/default.aspx?pid=233&trg=MainArea_5661&MainArea_5661=5565: 0: 15,4217: 1: 0: 0: : : 0: 0).
17. Næss O, Søgaard AJ, Arnesen E, Beckstrøm AC, Bjertness E, Engeland A, et al. Cohort profile: cohort of Norway (CONOR). *Int J Epidemiol* 2008; **37**: 481-5.
18. CONOR (The Cohort of Norway), Norwegian Institute of Public Health, Oslo, Norway. (http://www.fhi.no/eway/default.aspx?pid=238&trg=MainLeft_5853&MainArea_5811=5853: 0: 15,2818: 1: 0: 0: : : 0: 0&MainLeft_5853=5825: 56612: : 1: 5857: 2: : : 0: 0).
19. Utne H. The Population and Housing Census Handbook 2001. Statistics Norway, Department of Social Statistics, 2005/2 (http: //www.ssb.no/english/subjects/02/01/doc_200502_en/doc_200502_en.pdf.)
20. Furu K. Establishment of the nationwide Norwegian Prescription Database (NorPD) – new opportunites for research in pharmacoepidemiology in Norway. *Norsk Epidemiologi* 2008; **18**: 129-36.
21. The Norwegian Prescription Database, National Institute of Public Health (http://www.fhi.no/eway/default.aspx?pid=233&trg=MainArea_5661&MainArea_5661=5565: 0: 15,3791: 1: 0: 0: : : 0: 0&MainLeft_5565=5544: 50553: : 1: 5569: 10: : : 0: 0)
22. WHO Collaborating Centre for Drug Statistics Methodology. ATC Classification Index with DDDs, WHO Collaborating Centre for Drug Statistics Methodology, Oslo, 2006.
23. Guidelines for ATC classification and DDD assignment. WHO Collaborating Centre for Drug Statistics Methodology, Norwegian Institute of Public Health, Oslo, Norway.
24. NAV. Mottakere av uførepensjon etter diagnose, alder og kjønn (http://www.nav.no/184797.cms).
25. Olsen TS, Kvåle G, Jentoft N. Mellom trygd og arbeid. Motivasjon og risiko i uføres betraktinger om å gå tilbake til arbeidslivet. FoU-rapport 1/2005. Agderforskning (på oppdrag for det Norske Arbeids- og sosialdepartement) (http://www.agderforskning.no/reports/fou05_01_mellom_trygd_og.pdf).
26. van Hulten R, Isacson D, Bakker A, Leufkens HG. Comparing patterns of long-term benzodiazepine use between a Dutch and a Swedish community. *Pharmacoepidemiol Drug Saf* 2003; **12**: 49-53.
27. Isacson D. Long-term benzodiazepine use: factors of importance and the development of individual use patterns over time – a 13-year follow-up in a Swedish community. *Soc Sci Med* 1997; **44**: 1871-80.
28. Neutel CI. The epidemiology of long-term benzodiazepine use. *Int Rev Psychiatry* 2005; **17**: 189-97.
29. Gustavsen I, Bramness JG, Skurtveit S, Engeland A, Neutel I, Morland J. Road traffic accident risk related to prescriptions of the hypnotics zopiclone, zolpidem, flunitrazepam and nitrazepam. *Sleep Med* 2008; **9**: 818-22.
30. Cimolai N. Zopiclone: is it a pharmacologic agent for abuse? *Can Fam Physician* 2007; **53** : 2124-9.
31. Mellingsaeter TC, Bramness JG, Slordal L. [Are z-hypnotics better and safer sleeping pills than benzodiazepines?]. *Tidsskr Nor Laegeforen* 2006; **126**: 2954-6.
32. Bachs LC, Bramness JG, Engeland A, Skurtveit S. Repeated dispensing of codeine is associated with high consumption of benzodiazepines. *Norsk Epidemiologi* 2008; **18**: 185-90.
33. Skurtveit S, Furu S, Bramness J, Tverdal A. Benzodiazepine use in all alcohol consumers predicts use of opioids in patients 20 years later – a follow-up study of 13 390 men and women aged 40-42 years. *Pharmacoepidemiol Drug Saf* 2008; **17**: 926-33.
34. Søgaard AJ, Selmer R, Bjertness E, Thelle D. The Oslo Health Study: The impact of self-selection in a large, population-based survey. *Int J Equity Health* 2004; **3**: 3.
35. Nielsen MW, Søndergaard B, Kjoller M, Hansen EH. Agreement between self-reported data on medicine use and prescription records vary according to method of analysis and therapeutic group. *J Clin Epidemiol* 2008; **61**: 919-24.