Supplementary Table 2. Summary of all the Included register-based studies assessing long-term use of BZDs and/ or Z-drugs among the general population (all ages), adolescents and aged users.

|  |  |  |  |
| --- | --- | --- | --- |
| **Country, region, study period, the possible name of the study (Reference)** | **Aim of the study related to the assessment of long-term BZD use** | **Description of the methodology:**1. **Study population**
2. **Design**
3. **Register(s) used in the data collection and information collected**
4. **How BZD use is assessed**
5. **Authors’ key discussion point related to methodology**
 | **Key findings related to long-term BZD use** |
|  Norway, countrywide,1st January 2004 (baseline) - 31st August 2009. The inclusion period was the year 2005 Follow-up period was between 1st January 2006- August 2009 (1 274 days)(45) | To assess the course of the treatment among incident users during a 3.5 year follow-up period | 1. General population in Norway. Incident BZD users (n= 151 079).
2. Retrospective register-based study
3. Statistics Norway linked data from 1. Norwegian Prescription Database (NorPD) by the Norwegian Institute for Public Health, containing data on all dispensed prescription drugs from all Norwegian pharmacies since 1st January 2004. 2. Regular General Practitioner Database at Norwegian Social Science Data Services containing monthly updated data on individual GP’s patients (age and gender), GPs’ unique prescriber code.
4. Generic name of the dispensed drug, ATC code, strength, number of dispensed packages and DDD were obtained. The drugs were divided to anxiolytics N05B or hypnotics N05C. Only oral formulations and medicines approved by Norwegian Medicines Agency in 2005. The total volume in DDD during the study period since the index date was summarized per patient.
5. This was the first study assessing the initiation of BZD treatment by prescriber groups. Limitations: Different prescriber groups may be confounded by indication. No data about inpatients, prescribed daily dosage or indications, prescribers’ whole working field and drugs bought illegally. Incidence rate may be to high due to only one year baseline period
 | Of incident users, ~38% received anxiolytics, ~58% hypnotics and ~3% both. Initial anxiolytic prescriptions consisted mainly for long acting BZD ~ 56% and 44% of short acting ones. The initial hypnotics were mostly Z-drugs. During the follow-up, ~31% of the study population received BZD for short term, ~ 12% for long-term (redeemed prescriptions in a row for three quarters a year) and ~1% was heavy users. Long-term users often redeemed both anxiolytics and hypnotics. Key predictors for long-term use were: total drug volume redeemed during the first quarter (strongest predictor), increase in patients’ age, treatment initiated by psychiatrist, a young physician or physician with large overall drug prescribing volume or initial prescriptions for alprazolam, flunitrazepam or nitrazepam. According to separate analysis only conducted among GP’s the number of patients in GPs waiting list was the strongest predictor of long-term or heavy use. |
| Norway, Countrywide2004-2007 (46) | To examine the amount and frequency of redemptions of BZD naïve patients to assess the degree of dose escalation and the effects of risk factors on dose escalation. The factors were with clinical significance  | 1. BZD naïve patients, who had no prescription (Rx) fills prior to July 2004 for any BZD drugs (n=81 945), aged 18-67 in 2004.
2. Observational, retrospective study
3. NorPD (see description in study 45). Patient’s age, gender, physicians’ specialty, date of redemption, numbers of DDDs. The risk factors studied were age, gender, first BZD redeemed and previous use of drugs, prescribers’ prescribing volume and specialty.
4. The included BZDs were diazepam, oxazepam, alprazolam and nitrazepam and also Z-drugs zopiclone and zolpidem. The included patients had a first Rx between 10 and 30 DDDs and average daily dose < 1 DDD/day during the first 3 months. The dispensing data of chronic medications was a proxy for co-morbidities.
5. The first study on BZD naïve patients assessing excessive use. Only six months period was used to assess the time without BZD use. Dose escalation was the only indicator for drug dependence.
 | Most of the patients had zopiclone or zolpidem (63.8%) as the initial drug, followed by diazepam (25.3%) or oxazepam (6.1%).23% of the participants redeemed Rxs and 34% stopped using BZDs after the 3 months period. Many patients had intermittent use, and at three years follow-up point ~24% still used BZD and about 77% had stopped the use. The risk of dose escalation increased over time, but only 0.9% of the participants became excessive users (n=749). Long-term users with previous antidepressant, antipsychotics, opioid use, alcohol or smoking cessation treatment had a higher risk to become excessive user. Patients starting with oxazepam had a higher risk of becoming excessive users compared to diazepam users. A specialist in general practice as first time prescriber was associated with a lower risk compared to prescribers without specialty.  |
| Norway, Nord-Trøndelag -county. The HUNT cohort study. Data drawn from nationwide register13 years follow-up 1995-2008(48) | To identify factors associated with later BZD Rx:s including clusters of personality traits, self-esteem characteristics (2013), sleep difficulties, depression and anxiety symptoms and alcohol outcomes (2012).  | 1. Cohort formed from the general population in the Nord-Trøndelag county, aged ≥ 20 years (n= 58 967) and using BZD or Z-drugs
2. Prospective cohort study, combining NorPD and participants’ interviews
3. Outcome data was from the second and third wave of the study (2006-2008). This data was merged with the NorPD database (see study 45).
4. The BZDs and Z-drugs were defined according to the classes in the ATC classification system. Z-drugs and BZDs were combined. The associations between BZD use during study period and sleep data, anxiety, depression and problematic/non-problematic alcohol use in the HUNT 3 (2006-2008). Different forms of use were defined as follows: chronic Rx were for two or more consecutive years without a pause, intermittent ones were for two or more years but with a pause of at least one year during the four year follow-up. BZD dosages were defined according to the DDDs used. ≥ 180 DDD total in a year was a high dose of use
5. The combination of large, long-term cohort study and longitudinal data from the prescription register. The study did not differentiate between long- and short acting BZDs. No information of the prescriptions of the cohort members during 1997-2004, as NorPD was established in 2004.
 | Totally 13 774 individuals (23% of the sample) received at least one BZD Rx during 2004-2008. Zopiclone, oxazepam, and diazepam were the most commonly prescribed BZDs. Females were most likely to be prescribed chronic BZD courses. The likelihood increased by age. Older individuals were also more likely to receive high dose BZD. Among the study population 42% had a chronic use pattern, 10% became chronic BZD users with the use of several years without a pause. 18% used BZD with the high dosage of ≥ 180 DDD/ year BZD use was associated with nearly 3-4 fold risk of reporting severe anxiety outcomes. BZD use was related to nearly twice the risk of self-reported severe depression symptoms and sleep problems. Different clusters of personality traits and psychological symptoms were associated with different kinds of later BZD Rx patterns and dosages. Combination of high extraversion and neuroticism appeared to be a high risk profile for long-term BZD use in the initiation phase. Sleep difficulties, low self-esteem, high depression and anxiety scores were associated with later BZD Rx and with chronic and high dose Rxs.  |
| Norway nationwideJanuary 2004- October2009, (44) | To describe basic pharmaco-epidemiological patterns of BZD use in Norway. These are incidence, 12 month prevalence, mean volume used and duration of use | 1. All Norwegians, outside institutions, age ≥18 years
2. Retrospective register based study
3. NorPD database. Information on patient: gender, year of birth, place of residence. Information on prescriber: type, gender, profession and medical specialty. Data on dispensed drugs: strength, amount and date of dispensing.
4. The data for this study was obtained from all the licensed BZD Rxs. The drugs prescribed in institutions or given directly by physicians were not included in the analysis (~10% of all BZD Rx). The rate of BZD use, prevalence and incidence rates, rate of new users and mean volume used were calculated.
5. Complete capture of all Rx’s filled in Norwegian community pharmacies. No information of the real use patterns: low dose for long-term or episodic use in diseases with fluctuating characteristics?
 | About 260 000 Norwegians receive Rx for BZDs annually, (6% of the whole population). Many BZD users fill Rx for BZD very seldom. It was likely that the incidence fell down about 10% annually. The mean volume was stable and the vast majority of the users did not vary their use over time. The average mean volume used was 0.3DDD/ day among those filling at least two prescriptions. The average dose for females was 0.28DDD/day and for men 0.39DDD/day. The incident users used with a lower dosage than previous users. On average BZDs were used between 9 and 15 years (based on mean volume used), with longer durations for the higher volume users. The mean age among prevalent long-term users (> 1 year) was 62 years, and among incident long-term users 57 years. During a year about 25 000 of the 55 000 incident users fill two or more Rx. ~ Half of all the users BZD are prescribed for > two years.  |
| Sweden, local Tierp municipality ,1976-1989 (66)  | To analyze individual use patterns among long-term users (daily, frequent, infrequent, occasional). To assess in more detail the quantities obtained for predicting LTU  | 1. Longitudinal study in a 20 000-strong Swedish community, Tierp. A sample of BZD users in 1976 were followed for 13 years. The sample was limited to one fourth of the initial BZD users in 1976 (n= 2 038). The persons, who bought BZDs in the following years remained in the cohort. In the last year 1989, only the continuous users remained in the cohort
2. Retrospective, longitudinal study
3. Data was obtained from the Rx dispenses in two pharmacies in the Tierp community. Each Rx including refills were individually recorded
4. Users of different types of BZDs was grouped to three categories: tranquilizers (diazepam and oxazapam), hypnotics (nitrazepam) and combination of tranquilizers and hypnotics. For each dispensed drug DDD and annually a theoretical average use/ day/ person were estimated.
5. The theoretical DDD use was utilized for assessing the level of the actual use. Level of lost to follow-up may have influenced on the findings. The study was based only on the data of the purchases from the two pharmacies in the community and not those outside these pharmacies or illegal use.
 | The overall proportion of BZD users was slightly over 10%. Of the cohort members 65% continued to use BZD during the first year, 55% during the second year, 10% developed long-term use for 10 years ( n= 119) and a quarter of the long-term users (n=54) continued the use during the whole 13 years follow-up. Many of the initial users who discontinued the use in the first year turned up to new users. The pattern of use (daily, frequent, infrequent) remained mostly similar during the study period. The most important predictors of the long-term use of BZDs: frequent and daily use, quantity used, combined use of tranquilizers and hypnotics, increased age and previous use. Patients receiving the Rxs from physicians working in hospital or in in primary care or receiving Rxs from more than one prescriber type were more likely to use BZD long-term. Type of BZD or generic brand had no difference to the rate of long-term use. |
| Netherlands, nationwide (sample drawn from the National Network of family practices),The Benzoredux-study 1998-2001 (40) | Whether long-term BZD users in Dutch primary care increase their dosage over time | 1. The entire control group in a large BZD reduction study. Long-term BZD users, (using BZD > 6 months) selected from 19 Dutch family practices. During the study the family practitioners were unaware that their prescribing data was observed. The long-term-users were either incident (not using BZD 6 months prior baseline) or prevalent users.
2. Retrospective database study
3. Database of Dutch National Network of Family practices, from which data on BZD prescribing (recorded Rxs) was drawn from the electronic medical dossier (EMD) as used by most family practitioners. Patient data contained gender, date of birth and system identification number.
4. BZD doses in DDDs in the database were converted of PDDs (10 mg of diazepam = 1 PDD). The dosage during the first three months period was defined as baseline and the change in dosage during the next eight three month’s periods were followed. Differences between incident and prevalent BZD users were assessed. Patients with Rx < 180 PDDs during the three first months were considered normal dose users.
5. Large group of subjects with clear long-term use and sufficient period to follow-up. The actual intake was not measured.
 | No clinically relevant differences were observed between initial and previous BZD users.The BZD dose did not increase among either of the long-term users’ groups, incident or prevalent, suggesting tolerance to BZD to be rare.The key differences between normal and high dose users were: combination use of anxiolytics and hypnotics, type of BZD used and use of antidepressants. These were all more common among high dose users. High dose users were more commonly younger, used combination of BZDs and were not solely using hypnotics.  |
| Netherlands, nationwide (members of state insurance scheme)January 1999- December 2004  (37) | To gain more insight in prescribing BZDs or antidepressants (AD) in Netherlands. A specific aim was to assess if there is an association between patient categories and the number of or Rx to BZD or ADs. To assess the trend in repeat BZD prescriptions? | 1. Persons ≥ 45 years old, registered with two insurance companies for the whole six year period. The included persons are covered by compulsory health insurance under the Dutch state insurance scheme.
2. Longitudinal cross-sectional register-based analysis (cohort study)
3. Registers of two insurance companies. Includes all Rxs, using ATC classification. The database has following disease- specific subcategories: diabetes, pulmonary, or cardiovascular disease and multi-morbidity, which was validated by including only patients receiving Rx in each of the six years. Data of age and sex was included.
4. BZD and antidepressant (AD) prescriptions were based on ATC codes. Cross-sectional analysis to assess whether the four classes of patients differed in their BZD or AD use in 1999. A longitudinal analysis was conducted for BZD/ AD incident users. The number of years with 6-12 Rx for BZD was used to assess the length of the long-term BZD use
5. The reference category (patients without the Rx for the named conditions) was artificial, as the authors were unsure of the reference persons’ chronic conditions. The indicator for disease was relatively crude and indirect to assess the presence of a condition.
 | For assessing long-term use the authors assessed the frequency of persons with 6-12 BZD prescriptions / year according to number of years of having so many Rxs. Among patients belonging to multi-morbidity conditions (n= 37 534) 3% and 2.7% of the cardiovascular patients and 2.4% had received BZD Rx for 6-12 times a year during 5-6 years. The persons having diabetes were in the lowest risk. About 87% of the multi-morbidity, 89% of the cardiovascular and pulmonary, 93% of the diabetes and 94% of the reference category patients had not received 6-12 BZD Rx during any year.  |
| Netherlands, countrywideJuly 1998- June 2000 (38) | To determine whether hospitalization induces initiation of BZD use and subsequent long-term use. The period of consecutive use was calculated and the possible association between hospitalization and long-term use evaluated | 1. Randomly selected patients (n= 8 681), hospitalized during study period and an equal number of non-hospitalized controls. Inclusion criteria: adequate medication data available 18 months before and after the index date (=hospitalization), no BZD use 6 months prior index date.
2. Retrospective follow-up study (case-control)
3. PHARMO record linkage system containing all computerized pharmacy records from community pharmacies. PRISMANT database: the hospital discharge diagnoses, admissions and discharges of all 950 000 community dwelling residents of 25 population- defined areas since 1985. The data from the two databases were linked by the personal identification number. Patients were individually followed up until the estimated duration of the use of last BZD RX (max 6 months follow-up).
4. ATC classification system for BZDs and Z-drugs zolpidem and zopiclone was utilized. Primary outcome was the initiation of BZD use which was determined as 18 months before or 18 months after index date. Long-term use was a period of consecutive use of at least 6 months following initiation
5. The controls may be healthier than cases, as they were gathered from the users of any medicine; stratification of the chronic diseases in both groups.
 | During the entire study period the incidence density of initial BZD Rx in hospitalized patients was 11.8/ 100 patient years and among non-hospitalized it was 6/ 100 patient years. The incidence of BZD use was twice as high among the hospitalized patients.Predictors for new BZD Rx were: more diseases, age ≥ 65 years, longer duration of hospitalization. The three month time window before and after hospitalization and the initiation of new BZD therapy had a strongly significant association. The relative risk for long-term use (≥ 180 days) during the 36 months period was slightly higher among hospitalized than non-hospitalized patients (58.5% vs 56.2%). However, in three months’ time window pre and post hospitalization the RR for long-term use was much higher for patients not-hospitalized. The authors found no evidence for hospitalization being a risk for long-term BZD use.  |
| Netherlands, local, distinct area in the northwest of the Netherlands, Joure community 1984 -1992  (39,44) | To evaluate changes in usage patterns of BZDs in a stable population (1998). Different measures of prevalence of BZD exposure and evaluated exposure to individual BZDs over time. To identify initial pharmacy-related predictors of prolonged BZD use | 1. Study participants lived in a geographically concise area, Joure community of approximately 13 500 inhabitants during the whole follow-up period. For the study (2003) a cohort of 425 eligible adults (≥ 18 years old), who received Rx for BZD in 1984 and had not used BZD for 365 days before the index date was formed.
2. Retrospective cohort study
3. Pharmacy records of the study pharmacy was the data source for BZD dispensed during 1983-1992. Dutch pharmacy records contains nearly all information of all Rx drug use. The database contained information on the name of the drug, generic name, dosage, length and instruction for use.
4. BZD was defined as the ATC classification to those N05BA, N05CD, N05CF, N05CG. Prolonged BZD use was the key outcome variable. Total number of outcome years and dynamics of the change over time in BZD use. Prevalence and the estimated number of DDDs.
5. During the study period the overall figures were stable to assess the trends in BZD use. Cumulative exposure was assessed, which can be influenced by a variety of sources of inaccuracy. During the next two years following the initiation phase a significant proportion of the study participants either died or moved away.
 | Of the 425 eligible persons in the first year 45 persons (10.5%) used BZD for more than 180 days (long-term). In the study (1998) the long-term users typically used of almost during the whole year. Utilization of different BZDs showed a consistent decrease in the use of long acting ones and increase in use of the short acting ones.Women were using BZDs twice more commonly than men. The Rx number among women was much higher, but the amounts in DDD were not. The amount of Rx also increased with age During the follow-up 114 persons started using BZD for at least year, resulting in cumulative use of 2-7 years. In the final follow-up totally 58 persons (14% of the cohort) used BZD for the whole 8 years period. According to the study 2003 prolonged use was associated with the initially high number of Rx during the first 90 days, age of the patients and initial use of hypnotic. The use as hypnotic had two-to three-fold risk of long-term use compared to use as anxiolytic. Increase in use during 7 years follow-up was associated with short initial period (< 15 days) and switch of BZD.  |
| Netherlands, regional Nijmegen area June/ July 1996- May/ June 1997 (12,43) | To assess the effect of employing various definitions and data sources of BZD use in open population (2002)To identify patient- related factors of long-term versus short-term BZD use (2004) | 1. Open population, both in the literature review in the study in Nijmegen area (age 18-75 years old) (n= 80 315). In the study (2004) assessing the differences in long and short term use the study population consisted of 122 short and 128 long-term users
2. Literature review, accompanied by an observational study at a prescription database (2002). In the study comparing the differences between short and long-term users’ interviews of psychosocial status was conducted in addition to prescription database.
3. Data was collected from a 32 general practices in Nijmegen Health area of BZD RXs. Totally 48 046 computerized BZD Rxs were converted to Rx records, compiling the prescription database. It was utilized for assessing the validity and operationalization of the different BZD use definitions.
4. BZD medicines belonged to N05BA, N05CD,N05CF and hypnotics to N05CD,N05CF& N05CG. The information on: use/non-use for each day of the whole Rx period, the issued daily dosage and number of tablets during the past 12 months
5. The method of data collection and definition operationalized is one the major sources of artificial differences in prevalence.
 | The observational period, setting and definitions influenced remarkably on the prevalence of BZD use. Long-term utilization definition of one year use was not influenced by the length of the observational period. The long-term use of one year seemed most robust when sex and age group proportions of the users in different observation methods were assessed. The authors were unable to find a systematic pattern in relation to BZD use of observation period. The testing in the compiled database revealed that the longer the observation period, the higher the prevalence. Long-term users were always included in the observation period. The authors recommended to assess BZD use prevalence during one year period and to define long-term use of at least six months use during a year. The need for uniform criteria for BZD use prevalence was highlighted. In the study (2004) assessing the differences between short and long-term users the logistic regression conducted showed that a diagnosis from one diagnosis category or 2-8 diagnostic categories (especially psychiatric diagnosis), avoidance coping style, loneliness, lower educational level, older age were related to long-term use.  |
| Comparison of Sweden, Tierp community (1976-1989) and Netherlands, Joure community1984-1991 See rows 5 & 9(68) | To compare long-term usage patterns of BZDs in a Dutch and Swedish community in different periods.  | 1. The included populations were drawn from geographically confined areas with drug-exposure of nearly all the population. The Swedish data is from the Tierp community of nearly 20 000 inhabitants (study 5). The Dutch data came from the Joure community with a population nearly 13 500 (study 9).
2. Retrospective two country comparison study
3. Data was obtained from the automated pharmacy records from the two communities. The two pharmacies in Tierp and one in Joure dispensed nearly all the Rxs of the population in the areas.
4. BZD users were either initial users in the index year or previous users
5. The comparison of the two communities is based on data gathered at different times. See other limitations related to individual studies (5&9)
 | In both the cohorts annual BZD use was nearly 10%The overall proportion left in the cohort at the end of the eight year follow-up was about 33% in the both communities. Continuous? Long-term use was associated with increasing age, previous versus new and heavy versus non- heavy use. Both the cohorts had remarkably similar patterns in the follow-up, when the survival was stratified by different explaining factors.  |
| France, regional, west coast region of France1st January December 31 2008(55) | To determine the proportion of long-term hypnotic Z-drug issued without face-to-face consultation and factors associated with such a practice | 1. Adult long-term users of Z-drugs, living in Loire-Atlantique or Vendee (n= 5 669)
2. Retrospective cohort study
3. From the French National Insurance system administrative database information on socio-demographics of the patient, medical records, characteristics of GP and information on the hypnotics
4. Hypnotics were characterized by market label, number of prescriptions in 2008, prescription date and issue date.
5. Data from administrative database, socioeconomic status and chronic conditions were assessed as proxy measures
 | 4623 of the participants had > 10 Rxs. In all of the cases only 17% attended a consultation at each date noted on the Rx. Of all the Rx’s the cohort members had received during 2008, only 34% were associated with a consultation. Rxs were more likely associated with a consultation if the patient had low socio-economic status, consulted a psychiatric within last 12 months and had a disorder with long duration or was older. If GP practice was located in rural area, or had long patient lists renewal without consultation was more common.  |
| France, regional Payes de Loire Region, February to July 2010(54) | To identify and characterize regular users of zolpidem and zopiclone in real life conditions | 1. French patients, dispensed at least ones zopiclone (= 46 152) or zolpidem (n= 61 636) between February and July 2010 among the population affiliated to the general health insurance scheme. Study comprised of study populations for either zopiclone or zolpidem, which were similarly selected.
2. Prospective cohort study
3. The general health insurance scheme of the Payes de Loire region, covering 87% of the French general population. The database provides information on patients, prescribing physicians, pharmacies, dispensed the drug, number of dispensations and dosage of dispensed drug.
4. In France hypnotics can only be dispensed for maximum of 28 days and are reimbursed. Latent class analysis was utilized to identify, which drug user classes the investigated patients belonged, prevalence estimation of each class and a probability estimate for an individual to belong in that class.
5. Drug databases lack actual use data, lack of clinical and socio-demographic data and information of illicit use. The study utilized dichotomized variables on prescribing, patient background and dispensing.
 | Of zolpidem users ~41% and ~47% of zopiclone users were regular users. Regular users for both drugs were on average ~64 years old, women, prescribers mainly GPs. Pharmacy or doctor shopping was very rare. 46% of zolpidem and 51% of zopiclone users had a psychiatric condition. Four clinical subtypes of zolpidem users were identified. The most prevalent was the subtype I (50%): absence of pharmacy/doctor shopping and GPs as typical prescribers, treatment following guidelines. The second most prevalent (27%) class II consisted of users who had mental disorder and their treatment did not adhere guidelines. For the patients in the class III the number of dispensations and dosages were higher compared to earlier classes, Rxs are mostly from specialists. The IV class was a minority (1%), representing a large proportion of either doctor or pharmacy shoppers. These persons were younger and they had higher average daily dose and more dispensations. Zopiclone users were described with a three class model. Class I was prevalent (60%), Class II was the second most prevalent (36%). Class III was a minority subgroup (4%), its members had most often “shopping behavior”. |
| France, regional southeastern France, 2005 (53) | e calculated the annualage-adjusted prevalence rates of subjects filling prescriptions for AX-HY at least once(to measure ‘overall use’) and at least six times (‘chronic use’), To assess the annual age-adjusted prevalence rates of subjects filling prescriptions for AX-HY at least once (to measure ‘overall use’) and at least six times (‘chronic use’).  | 1. Southeastern French people dispensed anxiolytic or hypnotic in 2005. The study population consisted of over 4.4 million inhabitants in altogether 158 cantons
2. Retrospective database- based study
3. Outpatient reimbursement database of general Health Insurance Fund of Southeastern France (PACA-CNAMTS) containing data on all dispenses of Rx drugs from community pharmacies. The National Institute on Statistics and Economical Studies gave information of social and demographic data, occupational category, proportions of unemployment, of inadequate housing, income supports for those aged 25 or being single-parent (indicators for standard deprivation) and mean annual family income. Rate of GPs per 100 000 persons in each canton. The age-adjusted rates of special reimbursement for chronic condition was an indicator for chronic morbidity.
4. Purchases of anxiolytics N05C and non-barbiturate hypnotics N05B1-N05B2 in 2005. The ratio of individuals with at least one delivery of an AX or HY and the ratio of individuals with at least six purchases of these medications was calculated (prevalence) use of six months.
5. The database covers about 70% of the population. No information of the indications of the AX-HY prescription.
 | 15.5% (n= 684 006) had at least one purchase of AX or HY in 2005 and 5.9% (258 731 persons) had at least six purchases (long-term use) of these drugs in 2005. Prevalence rates increased with age and were higher for women. Highest prevalence of choric use (25%) was found among subgroup of women 80 years or over. At the canton level among women chronic use of HY-AX was strongly associated with the prevalence of antipsychotic use and of subjects with a chronic illness, subsidized housing and the age of 45-59 years. Among men chronic use was associated with antipsychotics use and subjects with chronic illness but not with subsidized housing. Among both men and women chronic use was negatively associated with inadequate housing. There were significant differences between cantons in the prevalence of chronic use. AX-HY dispensing was most common in cantons, in which strong socioeconomic gradient is prevalent.However, chronic use was most commonly associated with prevalence of antipsychotic use and chronic morbidity. Age, somatic and mental disabilities are the strongest predictors of chronic use |
| Switzerland, countrywide, Jan 1st to June 30th 2002 (67) | To obtain new and reliable results on the prevalence of BZD use in Switzerland, as well as for specific subgroups and BZD prescription patterns of physicians in domiciliary practice | 1. 520 000 patients from three different geographic and cultural regions, corresponding to 10% of the Swiss population. Participants ≥ 15 years with a complete pharmacy record and least one BZD Rx during the six months period were included (n= 45 309, 9.1%)
2. Retrospective pharmacy dispensing database -based study
3. The Swiss Community Pharmacy Database, SGPD contains complete medication profiles of individual patients from a large proportion of the Swiss pharmacies from 1994 onwards
4. The data on patients buying one of the nine most frequently prescribed BZDs were included: alprazolam, bromazepam, oxazepam, diazepam, lorazepam, flunitrazepam, midazolam, triatzolam or zolpidem. They accounted for 84% of the total BZD turnover in 2002
5. Not all but the most important BZD use was analyzed, no information on indication was given in the prescriptions.
 | For patients with the age of ≥ 65 years the prevalence of BZD use was ~32%. The authors calculated the one year prevalence rate to be 14.5%. 44% of the study participants had a single BZD Rx (n= 45 309) within the six months follow-up and the majority of the single users (83%) used BZD for less than 90 days. 56% had at least two Rxs during six months.Majority of (69%) patients in the repeated Rx group used BZD for more than 90 days. In both groups the majority of the patients used BZD in lower than the recommended dosage. Among the repeated Rx group, 6.6% used BZD with a dosage exceeding the recommended dosage max twice and 1.6% used it with a very high dosage, exceeding the recommended dose twice or more. The most problematic BZDs were lorazepam and alprazolam in regards to use of high and very high dosages.  |
| Germany, regional North-Germany, Hamburg region, 2005-2007 (61 | To determine the extent of the problematic prescription of BZD and non-BZD | 1. Persons living in Hamburg, Bremen, and Schleswig-Holstein Regions and using BZDs during an individual period of 12 months after the first dispensed BZD (n= ~78 500)
2. Prospective cohort study
3. North-Germany Pharmacy counting center (Nord-Deutschen Apothekenrechenzentrum, NARZ). From the database information on patients age, sex, place of living, prescriber, pharmacy. The database covers between 84% and 88% of all pharmacy dispenses in different cities.
4. On the investigated drugs information on one time dosage and the overall dosage, strength and number of dispensed medicines. 22 BZD drugs and three Z- drugs were included to groups of anxiolytics, hypnotics, antiepileptics and muscle relaxants. Individual daily dosage and the length of the use were calculated. The dosages were standardized in two ways: DDDs and the diazepam equivalent scales
5. The database covered about 88% of the dispensed Rx in the area. Data on three “Bundesländer”, may not be generalizable to the whole country
 | During the study period about 5.2% of all persons living in the Hamburg region purchased at least once BZD. A majority of them (83%) used BZDs according to the official guidelines. The patients usually purchased a dosage, which was between 77-85 daily dosages.Of the study participants from Hamburg 15.6% supplied BZDs with a long-term basis, exceeding the use of two months. Similarly, 19% from Bremen and 15.8% in Schleswig-Holstein used BZD over two months. Nearly 6% of the Hamburg patients were using BZDs with the riskiest way, use of over six months and daily dosage > 1 DDD or 10 mg of diazepam equivalent. ~ 8% used it with an amount that exceeded the use of six months. Most commonly BZDs were prescribed by GPs. Long-term use and the most problematic use were more common among persons 60 years and older than among younger persons. |
| Germany, countrywide (members of sickness fund) 2003-2004(60) | To seek patterns of high dose of zolpidem and zopiclone use. The aim was to seek durationof the use and dosage of the medicines and to investigate factors associated with their use. | 1. The population was drawn from 1.47 million German inhabitants belonging to the studied sickness fund. The included patients (n= 6959) had to stay as a clients of this sickness fund, were dispensed zolpidem or zopiclone at least once during all the four six-months study periods
2. Cross-sectional retrospective register-based study
3. From the sickness fund of Gmünder Ersatzkasse information on date of purchase, personal identification of the patient in anonymized form, prescribed medicines, the active ingredient, daily dosage, prescriber and dispensing pharmacy was obtained. Data of possible hospital stays because of psychological conditions, use of other psychotropic medications.
4. Z-drugs, duration, dosage, DDDs.
5. No information of indications with the exceptions of the hospital discharge diagnoses. The data was limited to Rx on sickness fund, no information on private Rx, among which high dose use can be even greater. No data of the factors causing the high-dose use. No causal relationship can be assessed.
 | The results from the first analysis assessing the use during six months period showed: Approximately every study person (n= 6 959) used 57 DDD during the investigated six months period. 3274 persons (47%) used Z-drugs for more than 30 days. Of these persons 32% for at least 60 days, 21% for at least 90 days and 15% for at least 120 days. Of the population 501 (7.2%) were high dose users. They were older, visited more physicians, used neuroleptics, visited physician only for gaining Z-drugs and suffered from polypharmacy. The use of zolpidem was more common among high dose users than the use of zopiclone. The sensitivity analysis did not alter these results.The analysis of two years development of the usage patterns was based on 6 171 persons. Of them about 10% were using with the highest level of use (from 2310 to 160 DDD). 30% of all the study population were using the drugs in all the four six-month follow-up periods. About 43% of the study population used at least 1 DDD daily. |
| South Africa, country-wide (members of sickness fund) 2004  (62) | To examine the prevalence of sedative/ hypnotic prescribing according to patient age and sex in a primary care setting. | 1. Patients from nine provinces in South Africa, suggested as a representative sample of patients covered by the private health care sector in South Africa
2. Retrospective cohort study
3. Electronic database of the South Africa private medical insurance administrator. The database contained Rx records of 37 804 patients.
4. All BZD Rxs including ATC groups N05BA, N05CD, N05CF were included. Measurement of use was defined as DDD and as prescribed daily dosage PDD. PDD was introduced to overcome the limitations of DDD use. Altogether 21 BZDs were investigated in this study
5. No generalizable information of the whole population in South Africa, as the sample was limited to the most affluent citizens.
 | Of the patients 8 084 received at least one BZD Rx during the study period. A majority of Rxs were prescribed for seven of the 21 BZDs investigated in this study. Duration of the use was calculated by the quantities of the dispensed units (tablets, capsules) per patient in each age group. BZDs were prescribed with larger amounts than BZD related drugs, the amount prescribed increased with the age of the patient. BZDs were prescribed for max 2 weeks period. However, there were 0.03 Rx for 70-240 units of BZD per patients between 41-50 years. For 31-60 units there were 0.033 non-BZDs per patient in that age group and 0.081 for patients in age group of 51-60.  |
| Taiwan, countrywide (sample drawn from the nationwide register)2000-2002 (50) | To investigate individual, service-provider and pharmacological factors accounting for different risks in the process from incident BZD use to long-term and discontinuation  | 1. Random, representative sample of from the general population members enrolled to Taiwan’s National Health Insurance program on Jan 1st 2000, responding nearly 1% of the Taiwan population.
2. Prospective follow-up study
3. National Health Insurance Research Database by the National Health Insurance Program, covering of ~ 98% of the population. In the study one subset of the National Health Insurance Research Database was utilized. Registries for beneficiaries, contracted medical facilities, drug files and medical claim data and data on prescribers were utilized.
4. All the 24 BZDs proved by the Bureau of National Health Insurance in Taiwan. The predicting variables explaining BZD use were either related to individual (age and comorbidities) service-provider (specialty, hospital level) and pharmacological (half-life, characteristics).
5. This study was the first to assess individual, service-provider and pharmacological characteristics of the investigated drugs. No data on possible confounders (bought via OTC or other persons’ Rx), patients’ compliance or lifestyle factors. The explanatory variables analyzed may not always precede the long-term use.
 | The prevalence of long-term use among the general population was 2.0-2.7%. Of the study sample, 10-15% of the individuals who received BZD Rx became long-term users. The rate of complete discontinuation among extensive long-term users was 4.77%.According to the results of logistic regression, male gender, age > 65, low income, existing of mental disorder, prescriber’s specialty of psychiatry, receiving prescription in hospital, number of BZD’s in the use, short half- life of the agent, combination of short and long acting agent, indication for hypnotic were most important predictors of long-term use. The factors related to pharmacological characteristics were most predominant in explaining long-term discontinuation of long-term use. Especially persons receiving short-acting BZD were at risk of becoming long-term users. Persons using BZD as an anxiolytic were more likely to have discontinued the use. Use of two different BZDs was associated with 30% lower likelihood of short term use than use of just one BZD.  |
| South Korea, nationwide(sample drawn from the nationwide register) 2007- 2011  (64) | To investigate prescription patterns of BZD of all adults in South Korea, including prescribing prevalence of > 1 day > 30 days, > 90 days, and 180 days, indication, daily dose and frequency of new Rx. | 1. Adult population in South Korea of ≥ 18 years, visited clinics or hospitals and had been prescribed at least one BZD during study period. For data analysis random sample of 5% of the patients for each year was drawn (n= 22 361 449)
2. Retrospective register-based study
3. Health Insurance Review and Assessment Service database (HIRA). It includes the medical and cost information of 97% of the population covered by national health insurance (NHI). Age, sex, reimbursable medications and diagnostic code by ICD-10. Type of treatment setting.
4. All the 32 BZD drugs reimbursed by Korean NHI during 2007-2010 were included. The drugs were divided to long-acting (n= 15), short-acting (n=13) and Z-drugs (n=4). DDD methodology was used to assess the dosage and duration of the treatment. The length was calculated by summing all BZD prescription periods in each year, these were categorized to classes ≥30 days, ≥ 90days and ≥180 days
5. The analysis based on the 5% of the population and their proportion was multiplied by 20. The validity and generalizability of this analysis was proven to fit all the population.
 | The average national prevalence for one year was 23.7% for ≥ 1 days, 7.9% for ≥ 30 days, 4.7% for ≥ 90days and 3.2% for ≥ 180 days supply. Among BZD users 19.7% were prescribed for ≥ 90 days and 13.3% for ≥ 180 days respectively. Among BZD new users 5.6% were prescribed the BZD for ≥ 90 days and 2.5% ≥ 180 days. A considerable number of patients receive Rx already in the initiation phase for long-term. The figures for patients in outpatient setting were 0.68% for ≥ 90days supply and 0.29% for ≥ 180 days supply among the whole South Korean populationThe average length of Rx for the non-elderly patients was 62 days and 129 days for the aged patients. The utilization trends during the five years follow-up period remained very similar. The most common indications were gastro-intestinal conditions in non-psychiatric departments, followed by psychiatric indications.  |
| Japan, local, outpatient clinics of Teikyo University Hospital July 2002- June 2003(65) | To examine characteristics of long-term BZD prescribing at a university hospital | 1. Adult outpatients, of the 19 department clinics in the university hospital, who were prescribed BZD during the study period only at one of the (n= 4239)
2. Retrospective dataset based study
3. Computer ordering system (COS) monitoring drug prescriptions in every clinical department at the hospital. From this data a new dataset of the patient information was created. Patients’ gender and age, specialty of the prescribing department, date of BZD Rx and characteristics of BZD.
4. BZDS were defined according to ATC classification. BZDs data was categorized according to the pharmacological half-life and BZD prescription. Long-term use was defined as use of at least 3 months.
5. Data of only the patients in one university hospital outpatient clinics cannot be generalized to the whole population, no data on dose or instructions for use.
 | 3 240 of the 4 239 patients were prescribed BZD for long-term basis. The authors did not calculate the prevalence rate but when the number of long-term patients were divided by the number of all patients receiving BZD Rx from single department, the rate was 76%.Long-term prescribing was associated with increased age and prescribing department. The mean age among long-term users was 9 years higher than among the short term users. BZD were more commonly prescribed at internal medicine and psychiatry clinic than at surgery clinic. Gender and pharmacological half-life had no difference. The result did not alter even though the authors analyzed the significance of pharmacological characteristics among the patients receiving BZD Rx from two or more clinics.  |
| Canada, regionalBritish Columbia cohorts of 1996 and 2006 (27)  | To examine whether use and long-term use of BZD had changed during 10 years period, with increased evidence on BZD harms. Differences in age and sex-specific rates of BZD use and long-term use.  | 1. All residents of British Columbia (BC), registered for the provincial health insurance plan in 1996 and 2006. The final cohort included 88% of BC population in 1996 and 92% of the 2006 population. The main analysis was carried out with the 2006 cohort data. 1996 data was used to describe population level changes in use over time and longitudinal use patterns.
2. Longitudinal prospective cohort study
3. PharmaNet: data on detailing Rx drug and medical services use records of every Rx dispensed outside acute care hospitals, the drug type, date of purchase and duration of the therapy (in days). Additionally, socioeconomic characteristics of the individuals were assessed.
4. Key outcome variable was the total BZDs Rxs duration for an individual BZDs or zopiclone. BZD related health status was measured, consisting of indicative of sleep disorders, anxiety/ neuroses or general psychiatric signs and symptoms based on Johns Hopkins University Adjusted Clinical Groups Case System mix to assess the overall health status. Number of different drug types an individual bought in 2006. ATC classification system was used. BZD users were categorized to non-users, short term users (< 100 days) and long-term users (≥ 100 days use) in a year
5. The study was able to detect age- and sex- specific development in BZD use. Key limitations: the measure of long-term use was based on days of Rx. The dosages represented by a day dispensed may be subject to change from 1996 to 2006. Pharmacy data indicated only dispensed medications.
 | In 2006 ~ 4.9% of the BC population filled BZD prescriptions that did not exceed 100 days and 3.5% filled prescriptions exceeding 100 days in total supply. The prevalence of long-term use among BZD users was not directly assessed. 49% of the long-terms users in 2006 were BZD users in 1996. Women were over twice more often than men buying BZD for short or long-term use. BZD users were generally older (especially in age group of ≥75 years), and belonged to the lowest income group. Long-term users had worse health status than short term users. When the age and health status were modified together, BZD long-term use was most likely in the age group 75+, women, with prescriptions from over 10 therapeutic categories and in the lowest income category. Diagnosed sleep problems, anxiety or psychological symptoms increased the likelihood of BZD use. The rate of BZD use and long-term use were higher in 2006 than in 1996, when it was adjusted according to the age and health status. There were also significant numbers of long-term users among the young or middle-aged.  |
| Canada, regional Saskatchewan  1979-1986 (34) | To measure the frequency and correlates of progression from the first BZD Rx to further Rx’s. | 1. Inhabitants eligible for coverage under the Saskatchewan Health Plan. Adults ≥ 20 years and filled at least one Rx for one of the five studied BZDs.
2. Retrospective cohort study
3. Saskatchewan Health Database: Health Insurance Registration file, the Prescription Drug Claim and the in-hospital database. Data on age, sex, new or repeat use and year of Rx was used.
4. Five studied BZDs: triazolam, flurazepam, oxazepam, lorazepam and diazepam covered over 90% of the BZD use in Saskatchewan. New users were defined as no use of any BZD 6 months prior the index date. Repeat user was filling three Rx for the same BZD during 5 months period. The definition was based on the format of dataset used.
5. The database covers over 95% of the Saskatchewan population. No information on lifestyle factors.
 | During the study period 225 796 persons had filled a Rx for at least one of the five BZDs. The new users’ cohort consisted of 225 545 persons. 23.5 % of them became (n=53 017) repeat users (at least three Rx during 5 months period). Repeat use was far more common among triazolam than oxazepam users and among elder persons. Women were prescribed BZDs more often than men but the risk of becoming long-term user was equal in both groups.The first prescription leads to repeated use especially among the elderly users. The probability of long-term use varied from 8 (20-29 years old) -40% (80+ years old) between different age groups  |
| US, regional, Western Washington State, January 1st to June 30th 1992 (56) | To assess the period prevalence of short-term and long-term use. To assess the patient characteristics and prescribing patterns associated with continued use among new BZD users.  | 1. Individuals belonging to Group Health Cooperative Puget Sound (GHC), HMO in western Washington state. All GHC members ≥ 18 years, staying in the GHC the whole six months follow-up. New BZD users (the new episode was by a prior interval of≥ 90 days prior the index Rx).
2. Cross-sectional retrospective cohort study
3. Computerized pharmacy records of GHC: patient age and sex were organized to examine prevalence of BZD use for specific groups. Additionally the authors reviewed the clinical records of 200 patients.
4. BZDs are defined as the generic names. Data on prescription dates, numbers of dispensed doses as number of pills. Cut point of 60 days daily continuous use was chosen for long-term use due to the form of the data base
5. The study was able to contribute to the picture of chronic BZD use. Medication use data alone cannot sufficiently judge the appropriateness of medicine use, clinical data is needed to evaluate the benefits.
 | Of the 240 946 individuals, 3.8% (n=7012) received during the follow-up at least one BZD Rx. ~25% of these BZD users were continuous daily users. Females were using BZDs more frequently than men. Among the new users only (n= 7012) 10.9% were chronic continuous users and for 75% BZD was prescribed 20 pills or less.The authors suggested that the six-month prevalence of continuous use was 1% among the general population. The factors associated with continuous use: being female, older age, BZD prescribed by psychiatric, although the psychiatrics are a minority in prescribing BZDs and GPs are the most commonly prescribing BZDs, prescription for lorazepam, alprazolam or triazolam, size of the initial prescription (> 30 pills). The most common indications were pain symptoms, anxiety and insomnia.  |
| US, regional New Jersey October 1987 to December 1990 (19) | To determine whether long-term BZD use is associated with dose escalation and patients’ characteristics related to it  | 1. Statewide sampling from three Medicaid populations: low-income mothers, elderly with poor income and disabled persons. The patients were using BZD for at least two years. They were initially prescribed BZD dosages within therapeutic range. Both incident and continuous users (n= 26 860).
2. Retrospective cohort design
3. Database containing drug dispensing and health care use data for all New Jersey Medicaid population. Data was received from the monthly enrollment records and drug and medical care claims. Patients with specific chronic illnesses were identified, based on ICD-9 criteria
4. Diazepam 20mg equivalent (=DME) dosages we defined for each BZD generic entity. The dispensed BZDs were converted to therapeutically equivalent DME dosages. All Rx during six months period / patient were aggregated and the average daily dosage was calculated. Dose escalation was defined by estimating linear time trends in monthly median BZD dosage after a three-month initiation period. Long-term use was the use of > 2 years
5. Medicaid Rx data is highly reliable and valid in measuring medication use, it is internationally consistent and stable over time. The method of converting BZD use to DME dosages has been validated. Large statewide sample of continuous BZD users of at least for two. Generalizability of the findings to other groups of long-term BZD users is unclear.
 | Among the 26 860 continuously enrolled patients, who received BZD at any time (in 1988) 3.2% purchaced a high dosage and 14.4% received BZD at least two years without an interrupt. 2 440 patients met the study inclusion criteria: 460 incident and 1 980 continuing recipients. A majority of them were women and white. A quarter had a diagnosis of chronic illness for which BZD was for.Long-term users were more often middle aged, had permanent disability or were treated for schizophrenia or depression. The median daily dosages remained constant. The dose escalation was relatively small, occurring only in 40 patients (1.6%). Further, none of the patients escalated the dose to very high level, of ≥ 100 DME. The escalation was more common among new users than continuous users.  Only regular use of short-acting high potency BZD lorazepam and being a pharmacy hopper were associated with dose escalation. |
| **Included register-based studies assessing long term use of benzodiazepines (BZD) or Z-drugs among the adolescents (n=1)** |
| Taiwan, nationwide 1999-2005 (51) | To understand the stability of and change in BZD use among incident long-term users over a five year period and to investigate predictors of variation in use patterns from adolescence to adulthood. | 1. Two age-groups of long-term users were identified, 1 758 aged 12-15 and 5 265 aged 16-19. The analysis was restricted to incident BZD users (no BZD prescriptions in previous year 1999)
2. Retrospective, longitudinal cohort study
3. National Health Insurance Research Database of the National Health Insurance Program in Taiwan. Data files of registered beneficiaries, contracted medical facilities, ambulatory care visits and drug prescriptions were combined. Medical institutions, where enrollees received BZDs were categorized to medical centers, district or local hospitals or clinics, clinics only and mixed. The specialties prescribing BZD were neurology, pediatrics, psychiatry or combination of them.
4. Altogether 26 pharmacological BZD agents were included. These agents were classified based on their a) half-life to short (< 20 hours) long (≥20 hours) or according to indication (anxiolytics, hypnotics). Dose was indexed by the average daily dose, which was calculated as total doses divided by the number of Rx days in 2000.
5. Large sample size, robust nature of the national health insurance data, first study to investigate trajectory patterns of BZD use among adolescents. The definition of long-term BZD use focused exclusively on Rx days. No distinction between intensive BZD users who received multiple BZDs within short period of time and those used BZD periodically. Only limited information about illness severity, clinical decision making, choice of agents and frequency of administration.
 | In 1999 among 11 to 14 years old adolescents 4.3% (n= 55 596) were incident BZD users and among the aged 15-18 were 6.3% incident BZD users. Within a year 3% of the users aged 12-15 and 5% of the incident users aged 16-19 became long-term users (prescriptions given ≥ 30days).Four distinct groups of the users, aged 12-15 years emerged: 58.4% were occasional (use < 30 days annually), 18.6% decelerating (use declined from 120days to 30 days annually), 7.8% accelerating (use increased from 30 days to 120 days) and 15.8% chronic users (use was consistently for 120 days to 150 days for the five year period). These four trajectory groups emerged also among the users of age 16-19, but the groups were different, for instance the 18.7% were chronic users.Between the short term and long-term users, key differences between variables related to patient, medical service providers or BZD pharmacology. Long-term users had more often received their Rx from psychiatry or BZDs in mixed form than short term users. History of psychosis (fourfold risk) or epilepsy (fivefold risk), prescriptions from psychiatry (three to four fold risk) multiple doctors of various specialties, long half-life BZDs or mixed indications significantly increased the risk of becoming chronic or accelerating user.  |
| **Included register-based studies assessing long term use of BZDs or Z-drugs among the aged general population (n=15)** |
| **Country, region, study period, if possible name of the study (Reference)** | **Aim of the study in relation to long-term BZD use assessment** | **Description of the methodology:**1. **Study population**
2. **Setting /design**
3. **Description of the register(s) used in the data collection**
4. **Matters related to the assessment of BZD use**
5. **Key methodological issue discussed by the authors**
 | **Key findings related to long-term BZD use** |
| Norway countrywide, 2008 (47) | To quantify inappropriate BZD-Z use in the Norwegian elderly according to a set of criteria derived from the guidelines and recommendations | 1. Community elderly of 70-89 years old, who in 2008 filled at least two Rxs for anxiolytic, hypnotic BZDs or Z-hypnotics. The sample consisted of 25% of all the Norwegian population of this age-group. Excluded were patients receiving medication for alcohol of opioid dependence.
2. Retrospective population based study
3. Norwegian Pharmaceutical Database NorPD (see study 45). Data on patients’ sex, age, prescribers’ ID, administrative codes indicating cancer or palliative care.
4. BZD use was described by: medication episode, sum of DDD/ week/ person. BZD use was defined inappropriate if one of the following conditions was filled: episodes lasted > 30 weeks, dosage was > 9 DDD/week/person. BZDs were divided to groups of anxiolytics, hypnotics and z-hypnotics
5. No information on institutionalized persons, dose used or time consumed was available. The definitions were used to separate the appropriate and inappropriate use and may underestimate the level of inappropriate use
 | Almost ¾ million RX for BZDs were filled in 2008 by just under half a million Norwegians aged 70-89 years old. A quarter of the Norwegian population of this age group received at least 2 RXs for these drugs. 12.3% of the study population (n= 57 276) older Norwegians used BZDs inappropriately.Long-term use was the most common form of inappropriate use. Over 70% of the study population had medication episodes lasting 30 or more weeks.Among the persons using at least two BZDs during the year 2008, over 73% of anxiolytic users, 76% of hypnotic users and 75% of Z-drugs users used the medicine longer than 29 weeks. 77.6% of the anxiolytic users, 25.5% of hypnotic users and 35.7% of Z-drug users used < 200 DDD/ year. The inappropriate use was most common among the subpopulation of Z-drugs users.  |
| Denmark, nationwide 1997-2008 (58) | To examine the pattern of use of BZDs and especially the association with age, comorbidity and socioeconomic status. | 1. All Danish residents ≥ 10 years on 1st Jan 1997 were included (n= 4 614 807). Focus on older people. Person who filled a BZD Rx in a given year was considered a BZD user in that year.
2. Retrospective cohort study
3. National Danish prescription registry. Information on all dispensed Rxs since 1995. Data on dispensing, quantity and strength and affiliations of the prescriber. Information was combined from the Danish National Patient Registry on all hospital admissions, primary and possible secondary diagnoses. Income information was obtained from the Danish national population registry.
4. Information on all claimed BZD Rx’s was used. Long-acting BZDs: chlordiazepoxid, diazepam, clobazepam, flunitrazepam, nitrazepam. Short acting ones: alprazolam, lorazepam, oxazepam, triazolam and Z-drugs. The intensity of BZD use was assessed by grouping BZD users to following classes based on daily-defined doses/ year: 0-30 DDD, 30-180 DDD and > 180 DDD/ year
5. Nationwide study, large dataset and high validity of the administrative database. Use of the register-based data as a proxy for drug use.
 | 1 480 017 (32%) filled at least one BZD Rx during the study period.The overall BZD use declined during from 12% in 1997 to 10.7% in 2008. Prevalence of BZD use and high intensity of use (≥ 180 DDD / year) was associated with increasing age, female sex and low socioeconomic status and with several comorbidities such as cardiovascular, chronic obstructive pulmonary disease and especially with depression and osteoporosis. The high intensity of use declined with increase in income.¼ of the persons aged 75-85 years and 1/3 of people over 85 used BZD in 2008. The risk for high intensity use ≥ 180 DDD/ year was 8.8 fold among those aged 85+ and 6.9 fold among those 75-84 years in age.  |
| Denmark, nationwide (sample drawn from the register)2003-2004 (59) | To estimate the degree of long-term Z-drug use among Danish women and men aged 65 years and older and associations with socio-demographic factors and use of other drugs | 1. A random sample of 5000 men and women from all the Danish residents in the age-group of ≥65. Their characteristics were assessed in 2003 and Z-drug use was followed during 2004
2. Retrospective cohort study
3. Information on purchased Z-drugs was drawn from the Register of Medicinal Product Statistics by the National Medicines Agency, containing detailed data of all purchases. Data was collected on: transmittal date, detailed ATC codes, strength, package size, number of packages and number of DDDs in the pack. ATC codes were used to assess the possible comorbidities. Data from Statistics Denmark was used to assess socioeconomic status. Drug use was used as a proxy for comorbidities
4. The Z-drugs available in Denmark were zopiclone, zolpidem and zaleplon. The data included > 10 000 Z-drug redemptions. Z-drug consumption was calculated based on the number of packages and the DDDs per pack. Z-drug consumption was assumed to be 0.5 DDD/ day. The analysis was also repeated with the use of 1 DDD. The durations were calculated as ≥4 weeks and ≥ 6 months use.
5. No information of the drug use during hospitalization was available, there was a lack of ATC codes of 3% of all the purchases.
 | 10% of the men (n=492) and 16% of the women (n=780) used Z-drugs in 2004. Among the persons redeeming Z-drug prescriptions in 2004, 94% of the male and 93% of the female used at least 4 weeks consecutive period. Furthermore 52% of the male and 58% of the female users were long-term users of at least 6 months. The risk factors for long-term use (≥ 4 weeks): being woman, high age, high income, widowed or divorced, high education or being disability pensioner and use of drugs in all ATC groups. The ATC group N drugs use was though associated with highest risk. The risk for the use of ≥ 6 months: high age, widowed or divorced and use of drugs in all ATC groups, but the highest OR was for the N-class (2.16). The high income and high education were not associated with long-term use of six months or more. 5% of the elderly had redeemed > ½ DDD/ day.  |
| Netherlands, local,Ommoor, suburb of RotterdamRotterdam StudyJanuary 1991- January 2003 (41) | To determine social and health related factors that predict new onset of chronic BZD use among the community-dwelling elderly.  | 1. Participants of the Rotterdam study, aged ≥57. Of the study participants 5 364 remained at risk for chronic use. 2 490 participants purchased at least ones BZD during the study period.
2. Prospective cohort study
3. Pharmacy records of seven pharmacies in Ommoord suburb, covering 90% of all Rx dispenses. The Rx records of the pharmacies were linked to a computer network, delivering online data of BZD Rxs. For each Rx ATC-code, dosage, prescribed daily dosage and number of tablets were recorded. Three domains: social support, health and perceived health and lifestyle factors were assessed by self-report questionnaires.
4. ATC classes N05BA (anxiolytics) and N05CD hypnotics were included. The BZDs were classified to short acting, intermediate acting and long acting ones.
5. The first prospective study, taking into account social and health related patient characteristics’ as determinants for aged people in the initiation of chronic BZD use. Rigorous selection of the population, BZD use was registered continuously and followed ten years. The key limitation: anxiety and depression symptoms were not classified according to DSM-IV.
 | The study identified 440 new cases of chronic BZD users. Of the 2490 participants who had filled at least one Rx for BZD ~18% became long-term users. Long-term users typically used the drug with low dosage ≤ 0.5DDD/ daily, 70% used short acting BZD and larger proportion used the drugs as hypnotics. At the index date 81% of the chronic users used short acting BZD. Key determinants of long-term use found in the Cox regression model among the whole sample: female sex, increase in age, high depression scores, sleep of < 6 hours, pain related complaints, hypertension experience of having poor health and current smoking. Among persons filled at least one Rx the determinants were having public health insurance, living in a service flat and having pain related complaints. Additionally, living alone protected from the long-term use.  |
| Taiwan, nationwide 2001-2010(49) | To characterize the 10-year trend in prescribing of Z-drugs among the elderly in Taiwan. Focusing on duration and dosages of the z- drugs prescribed.  | 1. Incident users (no use for two previous years) of Z-drugs, aged ≥65 years for each fiscal year were drawn from the utilized databases.
2. Population-based cross-sectional study
3. Ambulatory claims database of longitudinal health insurance database, NHIRD in Taiwan. NHIRD is a nationwide database comprising anonymous eligibility and enrollment information, visits, procedures and prescription medicine claims of more than 99% of the population (23 million) in Taiwan. The data of the population covered by Taiwan’s national reimbursement. In this study two subsets of NHIRD were used, from the years 2000 and 2005. These include ~10% of the population.
4. The investigated Z-hypnotics were zopiclone, zolpidem or zaleplon. For each Z-drug prescribed the information on initiation date (dispensing the drug), daily dosages, quantities and Rx duration were obtained from the databases.
5. The first study examining the in-depth association between patients’ and health care providers’ characteristics to Z-drugs use.
 | The number of patients ≥ 65 years in age increased to nearly three-fold from 2001 (=5 877) to 2010 (n= 17 591). On average each patient received 3.1 and 5.8 Z-drug Rxs annually. The most frequent (proportion in different years between 72-87%) duration of BZD Rx was 8-30 days. Most of the elder persons BZDs or Z-drugs were prescribed within the maximum daily dosage (≤one pill). The authors multiplied the most common duration (8-30 days) of the prescribed amount and number of Rxs (5.8 in 2010). As result most of the treatment episodes for elder persons were ~180days a year, suggesting a high rate of chronic use among the elder patients. Over 95% of the elderly patients were prescribed within the maximum daily dosage. The study provided no evidence that BZD use is replaced by Z-drugs’ use. |
| Taiwan, nationwide 2001-2002 (52) | To investigate BZD use and characteristics associated with usage among elderly outpatients in Taiwan | 1. Randomly selected 50 000 individuals from the eligibility files, comparable to all enrollees in the health insurance program. The program covers nearly 95% of the population in Taiwan. The persons of the age > 65 years in 2002 were included. The sample consisted of 4 267 aged persons.
2. Retrospective, observational study
3. A sampling database from the Bureau of National Health Insurance (BNHI) that randomly selected the sample. It contains information on ambulatory services records, hospital service records and prescription claim data and diagnoses by ICD-9 codes.
4. BZD use was characterized as the duration and dosage of the use. Mean dosages were divided to groups of ≤0.5 DDD, 0.6-1 DDD, 1.1-1.5DDD, or > 1.5 DDD. Durations were grouped to 0-0.5 months, 0.6-1, 2-3, 4-6 and 7 or more months. Previous BZD use was measured by the aggregated BZD use in 2001 and categorized as: no use, use of ≤ 30 DDD, 31- 120 DDD, and > 120 DDD. Prescription- overlap ratio was created to assess the level of Rxs overlapping in relation to the BZD covered days. Ratio > 0.2 indicated inappropriate use.
5. The study is based on secondary data, may contain inadequate or false coding, inadequate diagnostic information. Filled BZDs were proxy for use.
 | 1 826 of the persons included in this study received at least one BZD Rx in 2002. BZD use prevalence was 43%.Of the 1 826 persons 653 received BZD for 0-0.5 months, 210 for 0.6-1 month, 318 to 2-3 months, 249 for 4-6 months and 396 for 7-12 months. 22% of the BZD users took the drugs for at least 6 months period and 14% took a mean dose of higher than 1.0 DDD. Persons with insomnia, anxiety, depression or other mental health disorder were more likely to receive long-term BZD Rx and were in risk for long-term use. In addition previous BZD use was associated with the risk for long-term use and also use of higher dosages. Older individuals were less likely to receive high dosages but were more likely to use BZD for long-term. Persons with higher prescription- overlapping ratio were more likely to receive Rxs from multiple prescribers and were in higher risk of inappropriate use. |
| Canada, regional QuebecESA, Etude sur la Sante des Aines: Seniours’ Health Study 2005-2008 (31,32) | The prevalence of BZD use and frequency of potentially inappropriate Rxs among the elder population (31)To determine the source of incident long-term BZD Rxs by comparing the risk of receiving a new Rx upon hospital discharge versus after an ambulatory care visit (32) | 1. Members of longitudinal cohort study of older community-dwelling adults in the province of Quebec. 2 789 participants of ≥65 years in age, randomly selected and filled a mini-mental health assessment. All the participants included in the study of Halme et al (2013) were BZD free at baseline. There were 744 BZD users (32.1%) in the population (Preville et al 2012).
2. Longitudinal, retrospective cohort-study
3. Data of drug use was assessed by the Regie de l’assurance-maladie du Quebec (RAMQ), the provinces insurer. The RAMQ records contain all claims for medical service paid by the Quebec Medicare system. The pharmaceutical services records the code of the medicine prescribed, the quantity, dose, the dispensing dates and length of the treatment. This information was linked with data on hospitalization and with self-reported health data collected yearly during the study.
4. BZD use was measured by following indicators: the MDD index, the mean daily dose received during the year, measured in diazepam equivalents, the duration of the longest episode of BZD use during the year, the number of potentially inappropriate BZD Rx’s during the period (31). In the study of Halme et al (2013) the primary outcome was incident Rx of any BZD. Long-term use was any BZD of ≥90 days or more during a year (31) or 180 days (32) period.
5. The strength of the study was the linkage between register-based data and self-reported health data.
 | According to the study of Preville et al (2012) The BZD users used BZD with a mean daily dosage 6.1mg DZP equivalent and used BZD in average for 204.6 days during a year. 31% took the medicines < 91 days, 55% used for ≥180 days and 6.3% used BZD for whole a year. ~ 69% used BZD with ≥ 90 days episode during a year. The results from a logistic regression model show a significant association between respondents’ age, low income, number of prescribers and number of dispensing pharmacies and the number of days of BZD use during a year. The highest ORs was between the number of prescribers and long-term use. However, the majority (84%) of the study participants had only one prescribing physician.  19.8% took too a high dose of BZD at least once during the year. 3% used at least two BZDs simultaneously. In the study of (Halme et al 2013) there were finally 131 new BZD users (11% of the whole cohort). Of the new users 24 (18%) became chronic users. The incidence of new and chronic BZD use were 11% and 2% of the cohort. 5 users became chronic users during post hospitalization and 19 after an ambulatory visit. The risk for chronic BZD use was 2.7 fold higher per patient hospitalization than per outpatient clinic visit. |
|  Canada, Quebec 1998-2000 (follow up of one year per person) (36) | To compare factors associated with long-term BZD use by elderly women and men | 1. Eldelry, aged ≥ 66 years, men and women in Quebec living at home (n=1701)
2. Prospective cohort study utilizing data from Quebec Health Survey paired with data from health insurance plan
3. Quebec universal health insurance plan (RAMQ) on pharmaceutical, medical services and professional files
4. The length of BZD utilization was calculated by using the number of days between the first and BZD Rx delivered or a renewal Rx and the completion date of the last Rx. A delay of 15 days without renewal was defined as a sign of the end of the treatment period
5. The analysis strategy of assessing the association between physicians’ characteristics and respondents’ BZD use of the characteristics of the most visited physician may have reflected to the results. Large representative sample.
 | Women were more likely to use BZDs than men.74% of the prescriptions were renewalsAccording to the logistic regression model, the number of chronic physical health problems, number of physicians visited and the specialty of medical provider were associated with long-term BZD use in both samples. Respondents’ psychological distress level was associated with long-term BZD use in women only, whereas physician’s age was associated with long-term BZD use among men only. |
| Canada, Quebec 1989-1994 (28) | To characterize BZD use over time among elderly cohort of new users. Frequency of use of specific drugs, the rate of switching or adding medications and changes in dose over time and identify subject characteristics associated with the tendency of increasing dosage over time.  | 1. 78 367 community-dwelling Quebec residents aged ≥66 years in 1990, being new BZD users during 1990-1994 (not filling BZD Rx in 1989). Exclusion criteria: a temporary or non-unique health insurance number, death, non-resident in Quebec, long-term institutionalization in 1989, or living in geographically isolated region.
2. Prospective cohort study
3. Data was drawn from the Quebec Health Insurance Program on demographics (patients’ age, sex, postal code and date of death) medical services (type, location, diagnosis, treatment and referring a physician and date of all services), prescription claim of Rxs billed by the RAMQ (prescribing physician identification, American Hospital Formulary Service class, quantity, codes for substitution, renewal status, date of Rx and costs) and hospitalization databases (discharge diagnoses and date, admission date)
4. The start date, drug type, dosage, generic name, number of pills dispensed and duration for each Rx for each of the 11 BZDs available. These were used to construct the time-dependent measures of BZD exposure. The overall BZD exposure was assessed. Duration of distinct use was calculated for each Rx and a patient specific average duration. Standardized daily dosage was calculated for each Rx. For persons exposed to several BZDs overall daily dosage was calculated. The baseline data (1989) was used to assess predictors of change in BZD dose.
5. The longitudinal prospective, design allowed the authors to describe the complex patterns of BZD use among large cohort.
 | Almost half of the study population exceeded the recommended duration of 30 days. The average total duration was 7.5 months for an average observation period of 52.4 months. The average duration of a single treatment period was 30 days among 45% of the population. 20% of the new users used BZD between 31-65 days and ~ 9% used more. Still in 1993 the average duration of the first period of use was 60 days. The mean duration was longest among the users of temazepam or those using more than one BZD drug.Among the BZD users the mean dose corresponded the recommended half dose of adult population (0.57 DDD). About 8% of the users had a dose > 1 DDD. Older age, first prescription for alprazolam, oxazepam or clonazepam were associated with risk of increasing dosage over time. Men had an overall greater risk of increasing dosage. Though, the study detected a subgroup of older women, who tended to increase their dosage over time and use BZDs for long-term. The authors discussed whether older women are a subgroup more vulnerable for tolerance or having more severe psychiatric illness. BZDs appeared to be misused among a small proportion of the subjects. These patients exceeded the recommended duration of use and adult daily dosage.  |
| Canada, regional Ontario April 1st 1992 – March 31th 2005(33) | To estimate the rate of new chronic BZD use after hospitalization in older adults not previously prescribed BZD | 1. Individuals aged ≥66, discharged after acute care hospital admissions in Ontario (n= 405 128). Discharge date was the index date. Patients had to stay alive and not to have hospitalization 1 year before or 6 months after the index date. Patients with consultations with a psychiatrist or in palliative care were excluded.
2. Retrospective cohort study of population-based administrative data
3. The Ontario Drug Benefit database (ODB) records on all dispensed Rx medications. This data was linked with Canadian Institute for Health Information Discharge Abstract Database, containing data on all hospitalizations in Ontario. The Ontario Health Insurance Plan physician-billing database to gain information on inpatient and outpatient physician services. The Registered Persons database containing data on demographic and vital status of each citizen in Ontario.
4. The inclusion criteria were set to gain information on to describe the long-term BZD Rxs in a particular hospital discharge. The BZDs monitored in this study were divided to shorter and longer acting ones.
5. Extensive lifespan and considerations of more than 400 000 hospitalizations. Strict definition of chronic use required an initial Rx and to be linked with a subsequent one. The definition used for chronic long-term use however may diminish the prevalence of long-term use, as it required two prescriptions in two time points.
 | There were 12 484 early BZD users (BZD Rx already before 7 days since the discharge)29 207 late BZD users (new Rx 8 days and six months since the discharge)Altogether the study was able to detect 6 136 chronic BZD users (1.5%), suggesting that a half of the patients dispensed an initial BZD were also receiving a later prescriptions.During the follow-up period, the annual rate of new chronic BZD Rx decreased from 1.8% of the first year to 1.2% in the last year. Females, patients with ICU admissions, longer hospital stays, higher comorbidity and a diagnosis of alcoholism in the previous 3 years and were prescribed more medications were in increased risk for new chronic BZD use. Older individuals were less likely to receive chronic BZD prescriptions.  |
| Canada, Regional  Nova Scotia 1993-1996,  (28) | To study patterns of BZD use by Nova Scotia seniors. To explore the prevalence of BZD use, to determine the duration of periods exceeding 30 days | 1. Individuals aged ≥65 years and registered with the Pharmacare program and filled at least one BZD Rx during 1993-1996
2. Descriptive, cross-sectional population-based study
3. The provincial administrative drug database contains data on all persons insured under the Nova Scotia’s Seniors Pharmacare Program. The database contains comprehensive information on filled Rx, date of filling, quantity, days’ supply and drug identification number
4. BZD appropriateness was used by assessing Beers criteria on appropriateness of BZD for the elderly. For treatment duration, the parameter used was the periods exceeding 30 days duration.
5. No information on instructions for use or indication of the BZD. No assessment of incident versus prevalent users. Difficulties in assessing the true dosage. Some subgroups such as Indians or war-veterans are not included in the database.
 | The proportion of BZD treatments exceeding 30 days increased significantly during the study period from 65% to 68% (1993-1996). The overall prevalence of BZD use among seniors decreased significantly (from 18.6% to 16.8%). The proportion of seniors using BZD for 90 days or more declined from 11.4% to 9.6% during the study period. The estimated average daily dosage of BZD used by the elderly exceeded the recommended daily dosage except those using alprazolam, lorazepam, oxazepam or bromazepam.  |
| Canada, Regional British Columbia January - December 1990,  (30) | To describe BZD prescribing for elderly people living in the community in British Columbia and to compare such prescribing with an indicator of current guidelines | 1. All elderly (age of > 65 years) persons living in British Columbia (BC) and dispensed BZD in 1990
2. Descriptive study of pharmacy billing data
3. Pharmacare Plan A data on BZD dispensed to non-institutionalized elderly people. The data contained individual identifier, sex, birth date, date of filling the prescription, physician number, drug name and quantity
4. All BZDs and zopiclone. (Clonazepam was excluded as it is classified as an anticonvulsant in Canada). The amount of BZD used was calculated in diazepam equivalents. The definition given for inappropriate use was as maximum limit of 2-months for 20 diazepam equivalents, based on BC Drug Usage Review Program (DUR) in 1986.
5. The definition to inappropriate BZD use was found arbitrary. No information on daily dosages, intended duration or diagnosis.
 | BZD were dispensed to 24% of the non-institutionalized elderly in BC. The median number of Rxs dispensed to one person during the year was three. Four or more Rxs were dispensed to 41% of the population. 8.5% of the prescriptions were for more than 8 weeks duration. Single kind of BZD was dispensed to 80% of the population, but three or more kinds of BZD were dispensed to 3.3% of the population. Inappropriate BZD Rx, maximum recommended 2 month limit of BZD was prescribed to 17.1% of the patients. 10% of the BZD users received such Rx in all the five two month periods in 1990. According to the authors, 4% of the total population are prescribed BZD dosages and lengths above guidelines. Differences between prescribers: Physicians prescribed more frequently BZD ( ≥ 200Rx in 10 months) prescribed them in larger amounts. Men prescribed more and more often inappropriately than women.  |
| Canada, Quebec, Regional 1991- 1993February 1991- May 1992 CSHA1 screening and follow-up of each individual for one year after the screening (35) | To determine the prevalence and incidence of long-term use of benzodiazepines and to assess patient-, prescriber-, and drug-related risk factors | 1. 1423 community-dwelling older adults, age ≥ 65 years in Quebec who participated in the Canadian Study of Health and Aging Phase 1 (CSHA1) and had valid health insurance numbers. Only new users were included (no use 180 days prior the index date)
2. Retrospective Cohort study
3. CSHA1 database was linked with provincial health insurance data, RAMQ to which ~ 98% of the aged population is registered. Socio-demographic data, data on comorbidities, BZD use and prescriber characteristics (gender, year of graduation, being a specialist of generalist). In addition the data was linked with the CSHA1 clinical screening interview assessing cognitive and anxiety symptoms.
4. BZDs were divided to long or short acting ones and to hypnotics and anxiolytics. Only traditional BZDs. Use of BZD for at least 135 of the first 180 days (75%) following initiation of use was used as the definition for long-term continues use.
5. No information on hospitalized patients, although 8% of Canadian elderly patients are hospitalized.
 | One year prevalence of long-term continuous use, standardized by age and gender to the Quebec population, was 19.8 %. 20.8% of (n= 296) the study population had patterns of chronic continuous use. 959 were at risk for new long-term use. Twelve-month cumulative incidence of long-term continuous use was 1.9%. According to the logistic regression predicting long-term continuous use only patient age was found to be significant predictor of long-term use. The patients 80 years and over had the highest risk.  The logistic regression found no evidence that gender, health status, anxiety symptoms, cognitive status, benzodiazepine type, and physician characteristics would be related to the risk of long-term use. |
| US, regional Seattle, 1986-1992  (57) | To describe prevalence and incidence of BZD use during index year. Describe persistence and intensity of BZD use over a 4-year period and examine factors associated with BZD use in the upcoming year | 1. Random sample of men and women ≥ 65 in age (n= 1505) enrolled in a Group Health Cooperative, GHC, of Puget Sound, a large Health Maintenance Organization, HMO (for over 370 000 persons)
2. Retrospective cohort study
3. BZD exposure was defined from automated pharmacy files of the GHC. GHC included information of therapeutic class, drug form, strength, dispensing date and quantity. Data of the patients’ background was also received from mailed questionnaires obtained at baseline and in follow-up in 1st and 2nd years.
4. For each studied BZD a standardized dosage was calculated using the standardized intensity of exposure (TSD) methodology reflecting both dose and duration. TSD represents the number of days of use BZD over 1 year if used at a minimum effective dose. TSD use in the assessment yields longer usage periods as it expects the dosages lower than DDD. Based on TSD the use patterns were categorized to infrequent, occasional, frequent and daily.
5. The results may not be generalized to other elder populations as the HMO participants were healthy, white middle-class elder persons.
 | During index year the prevalence and incidence of BZD use were 12.3% (n=185) and 6.6% (n=94). After the index year 62%, 47% and 39% of the users in the index year used BZD in the consecutive years 1.,2.,3. 16% of the new users and 63% of the previous users continued the use for all following three years. The majority of the persons using during the whole four years’ (n=72) period were occasional users (about 50-63%/ year). The next largest group were daily users (21-18% / year). Infrequent users were the rarest class (4.2-8.3%/ year). The percent of daily users who used the drug for all the next three years after index year was 75% among new users and 92% for previous users. About 1% of the sample had evidence for the daily use of all the four years.The key predictors for use over one year were female, having a high school education, higher chronic disease score, higher level of self-reported stress and pain and self-reported nervous disorder at baseline. Overweight was associated with long-term BZD use. Previous use was the strongest predictor of long-term BZD use.  |
| Australia, regional South Australia and Victoria 2002 (63) | To examine to which extent BZDs are prescribed to elderly Australians | 1. Patients of ≥ 65 years from 29 GP practices in South Australia and Victoria (n= 3 970).
2. Retrospective database study
3. The Medical Enquiry Drug Information Centre, MEDIC-GP database, giving information on the GP practices described above.
4. Data on all BZD Rxs in 2002 were investigated. 13 BZDs, zolpidem and zopiclone were included. Text fields of the database were used to search these prescribed drugs by trade or generic name.
5. Prescribing database has the advantage over dispensing database to collect data on all Rxs, not just only reimbursed ones. The data may not be generalizable to all patients. Capture of all BZD Rxs may be incomplete.
 | 625 had at least one BZD Rx, prevalence 15.7%Of the patients prescribed BZDs 40% had only one Rx event, 45% had between 2-6 events and 15% had at least 7 Rx events (approximately six months daily BZD use). |