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***Original***

# Utilization of Psychotropic Drugs in Taiwan: An Overview of Outpatient Sector in 2000

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***Key Words***
defined daily doses (DDDs);
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psychotropic drugs

***Background.*** Development of pharmacological treatment in mental disorders has risen drastically over the past decade in Taiwan. We performed a survey of the National Health Insurance claims for outpatient psychiatric services to study the utilization of psychotropic drugs. The analysis followed the drug classification and standardized measurements proposed by the World Health Organization.

***Methods.*** The sampling datasets from the National Health Insurance Research Database served as data sources. They represented 0.2% of the entire claims for outpatient medical services in 2000. The measurement units used for psychotropic drugs were either prescription volumes (drug items) or the number of defined daily doses (DDDs). To estimate the proportion of the population treated daily with psychotropic drugs, numbers of DDDs per 1000 inhabitants per day were also calculated. Beside overall description, the data of psychotropic substance prescriptions were analyzed by stratifying patient's age, physician's specialty, accreditation status of hospital, and chemical subgroup of psychotropic drugs.

***Results.*** Prescription of psychotropic drug items (n = 63,539) was 3.24% of the total drug items (n = 1,958,820) claimed. The psychotropic drugs were prescribed to 9.2% of the total patients and in 9% of the total visits. Major consumers of psychotropic drugs were between 35 - 74 years of age and there were more women than men. The psychiatrist was the largest group of physicians who had prescribed psychotropic drugs and contributed 18.5% of all drug items and 38.3% of total DDDs of psychotropic drugs. The number of DDDs per 1000 inhabitants per day for all kinds of psychotropic drugs was estimated to be 32.94 in Taiwan, where anxiolytics accounted 14.30, hypnotics and sedatives 10.64, antipsychotics 3.41, antidepressants 3.06 and mood stabilizers 1.43. Ordered by total DDDs, the top 10 most frequently used chemical substances were flunitrazepam, alprazolam, fludiazepam, oxazolam, lorazepam, diazepam, zolpidem, estazolam, zopiclone, and haloperidol.

***Conclusions.*** The usage level of psychotropic drugs in Taiwan was lower than in most industrialized countries, especially for antidepressants. The future goals are to focus on the longitudinal analysis of general trend for each psychotropic substance and to associate the pharmacoepidemiological data in parallel with the upcoming epidemiological study of mental disorders in Taiwan. [*Chin Med J (Taipei) 2002;65:378-391*]

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Epidemiology is the cornerstone for medical science research and health policy making.[1] Epidemiological studies of the prevalence of mental illness seemed more difficult than studies on other medical diseases. Over the past 50 years, a series of studies on psychiatric epidemiology have been performed in Taiwan,[2-8] yet to yield no data regarding the drug utilization of drug treatment in the community was reported. Development of psychopharmacology has risen dramatically over the past decade, leading to a new direction of studies on drug utilization. Drug utilization was defined by the World Health Organization (WHO) as the "marketing, distribution, prescription and use of drugs in a society, with emphasis on the resulting medical, social, and economic consequences."[9] The objectives of these pharmacoepidemiological studies are relevant to problem identification and analysis, and decision making throughout the drug and health chain.[10] With the implementation of Taiwan's National Health Insurance (NHI) program covering nearly all the population on this island since 1995, the database regarding the diagnosis and treatment of mental illness became accessible and useful for analysis. The results would provide a clearer picture of pharmacoepidemiology in psychiatric disorders and help improve the policy making process on mental health.

In this current study, we performed a survey of national insurance claims for psychiatric outpatient services to study the psychotropic drug utilization. Our aims are to depict the distribution of the prescriptions of the psychotropic drugs and to compare the dispensing status associated with age and sex, between psychiatrists and other physicians, and among different medical facilities. The analysis followed the drug classification and standardized doses proposed by the WHO, in hope to have international comparisons in the near future.

## Methods

Normally a medical care institution under the contract with the Bureau of National Health Insurance (BNHI) in Taiwan submits its monthly claims in 3 files for outpatient services. One file (TOTFA: total file A) contains only one record summarizing the total monthly claims in an institution. Another file (DTLFA: detail file A) is the visit file record, which contains the summary for each visit. The third file (ORDFA: order file A) consists of the detailed prescriptions of both laboratory and drug items from every visit. The claims for inpatient services have the similar structures. The claims in the form of electronic data sending from all institutions are gathered into the data warehousing system of the BNHI after routine processing of reimbursement. Since 1999, all the claim data have opened up to the public for research use. For privacy protection, the identification data of patients and institutions had been scrambled cryptographically to attain anonymity. In the first few years the National Health Research Institutes (NHRI) was in charge of the huge database in size of terabytes under the project of National Health Insurance Research Database (NHIRD). Initially dozens of datasets had been extracted and released to satisfy the general needs of different researchers. By the end of 2001, data from 1996 to 2000 became available to the public.

In the current study, we used the sampling files of the year 2000 (S_CD20000 and S_OO20000 of NHIRD) for analysis. In the terminology of NHIRD, the database CD is defined as the collection of all visit files (DTLFA) from all medical care institutions and the OO is that of all order files (ORDFA). The two files (S_CD20000 and S_OO20000) were respectively extracted from the databases CD and OO in 2000 (excluding services of dentistry and traditional Chinese medicine) with the systematic sampling method. According to NHIRD, the size of the subset from each month is determined by the ratio of the amount of data in each month to that of the entire year. Then the systematic sampling is performed for each month to randomly choose a representative subset. A sampling database is obtained by combining the subsets from 12 months. The sampling database of S_CD20000 was constructed at first, and then the relative observations in S_OO20000 were drawn out accordingly. The sampling database of S_CD20000 was 0.2% to the original database in size (http://www.nhri.org.tw/nhird/) (ac-

**Table 1. Anatomical Therapeutic Chemical (ATC) Classification and coding structures for flunitrazepam**

| Codes | Remarks |
|---|---|
| N | Nervous system (first level, anatomical main group) |
| N05 | Psycholeptics (second level, therapeutic main group) |
| N05C | Hypnotics and sedatives (third level, therapeutic/pharmacologic subgroup) |
| N05CD | Benzodiazepine derivatives (fourth level, chemical/therapeutic/pharmacological subgroup) |
| N05CD03 | Flunitrazepam (fifth level, subgroup for chemical substance) |

cessed 24 December 2001). We also obtained a complete database of the approved drugs in Taiwan from the BNHI web site (http://www.nhi.gov.tw/) (accessed May 25th, 2001). Each drug of different brand, strength and form was officially assigned a unique code in the claims file. Another file (HOSB2000 in NHIRD) about the basic data of medical care institutions provides the status of accreditation: medical center, regional hospital, local hospital, and primary care unit.

Additionally, the Bureau of NHI offered a list of the Anatomical Therapeutic Chemical (ATC) codes for each drug. This ATC classification system was recommended by the WHO for drug utilization studies.[11] Structure of ATC code has five levels to divide the drugs into different groups and subgroups. Table 1 illustrates the ATC coding structure with an example of flunitrazepam. The psychotropic drugs are mainly classified under N05 (psycholeptics) and N06 (psychoanaleptics). Our study included all subgroups of N05 (N05A: antipsychotics; N05B: anxiolytics; N05C: hypnotics and sedatives) and parts of N06 (N06A: antidepressants; N06BA: centrally acting sympathomimetics; N06C: psycholeptics and psychoanaleptics in combination). The subgroup of N06D (anti-dementia drugs) and the other parts of N06B (psychostimulants and nootropics) were not included in our analysis because the majorities of this category were ginkgo biloba and piracetam. To reflect the current trend of psychopharmacologic therapy, we also included some drugs assigned in the category of antiepileptics (N03AE: benzodiazepine derivatives [mainly clonazepam]; N03AF: carboxamide derivatives [mainly carbamazepine]; N03AG: fatty acid derivatives [mainly valproic acid and dipropylacetamide]). Totally 1024 psychotropic drugs were collected for further analysis.

The WHO guidelines have also assigned a defined daily dose (DDD) to most chemical substances at the 5th level. DDD methodology was developed in response to the need to convert and standardize readily available volume data from sale statistics or pharmacy inventory data into medically meaningful units, to take crude estimates of the number of the persons exposed to a particular drug or class of drugs.[12,13] The DDD, the assumed average maintenance dose for the main indication of a particular drug, is expressed as DDDs per 1000 inhabitants per day. It can also be interpreted as the proportion of the population that may receive treatment with a particular drug.[11,14,15] The DDD thus serves as a unit of measurement for the longitudinal and international comparisons and does not reflect the actual prescribed daily dose.

The database software of Microsoft SQL Server 2000 was used for data linkage and processing to display. The regular descriptive statistics were displayed. The units of measurement for psychotropic drugs were either numbers of prescription items or numbers of total DDDs. There were 21,400,826 people insured under the NHI at the end of 2000. To estimate the proportion of the population in Taiwan treated daily with psychotropic drugs, we followed the international consensus and also presented the data as numbers of DDDs per 1000 inhabitants per day. The corresponding numbers of DDDs were at first extrapolated and multiplied by 500 (sampling ratio), divided by 21,400,826 (insured people) and 366 (days in year 2000), and then multiplied by 1000 (inhabitants) to gain the data for international comparisons. Beside the overall analysis of the files, we conducted similar analyses stratified by patient's age, physician's specialty, accreditation status of hospital, and chemical subgroup of psychotropic drug. ANOVA-R was used to compare differences of psychotropic drug prescriptions among age and gender groups and student t test was for comparison between

**Table 2. Summary of S_CD20000 and S_OO20000 datasets (0.2% sampling)**

| | All visits | Psychiatric visit | Visits with psychotropic drug prescriptions |
|---|---|---|---|
| Visit count[a] | 526,693 | 5,204 | 47,598 |
| Drug item count[a] | 1,958,820 | 17,410[b] | 63,539[c] |
| Patient count | 513,294 | 5,132 | 47,063 |
| Male | 230,154 | 2,479 | 19,564 |
| Female | 280,285 | 2,623 | 27,307 |
| Unknown sex | 2,855 | 30 | 192 |
| Patients' average age | 37.0 (SD 24.5) | 44.5 (SD 17.3) | 51.8 (SD 19.7) |

[a] The count numbers should approximately correspond to 0.2% of total count numbers within the NHI in 2000.
[b] Including non-psychotropic drugs.
[c] Including psychotropic drugs only.

genders at each age level.

# Results

## Data of all visit files (S_CD20000) and order files related to psychotropic drugs in 0.2% of the total samples

The visit file of S_CD20000 contained 526,693 records and the order file of S_OO20000 contained 2,574,739 records. These sampling datasets consisted of 513,294 patients and among them, 13,034 (2.54%) patients had more than one visit record. Among the medical specialties, the psychiatrists had contributed 5,204 (0.99%) records to the visit file of S_CD20000. It could thus be estimated that the NHI had approximately 2,602,000 psychiatric outpatient consultations in 2000. The patients who visited psychiatrists were in average 7.5 years older than all the patients (44.5 *vs*. 37.0 years, respectively). In addition, 9.2% (n = 47,063) of the total patients (n = 513,294) and 9% (n = 47,598) of the total visits (n = 526,693) were prescribed psychotropic substances. The mean age of the patients who received psychotropic drugs was at a mean age of 51.8 (SD 19.7) years - about 14.8 years older than all the patients and 7.3 years older than psychiatric patients, indicating more prescriptions of psychotropic drugs given to the older people who did not visit psychiatrists.

Table 2 also shows that among the total 1,958,820 prescription items of drugs in the order file of S_OO20000, 3.24% (63,539 items) belonged to the psychotropic drugs, which was defined in the methods section. These psychotropic drugs were prescribed to 47,063 (9.17%) patients in 47,598 (9.04%) visits. Each patient and visit was in average given 1.35 and 1.33 psychotropic drugs, respectively. Conversely, each patient visited psychiatric clinic received an average of 3.4 psychotropic drug items.

## Distribution of psychotropic drug prescriptions by age and gender

Table 3 shows the distribution of psychotropic drug prescriptions stratified by patients' age. The patients within the age groups of 35 to 74 years were the major consumers of psychotropic drugs. Although the patients older than 75 years took fewer psychotropic drugs collectively, their percentages of visits with psychotropic drugs in all visits were higher than those of other age groups (16.48% aged 75 to 84 years and 16.34% aged > = 85 years *vs*. < 15.5% of other age groups, respectively).

Among the 47,598 visits with psychotropic drugs, the male patients accounted for 19,786 (41.6%) visits, the female patients for 27,619 (58%) visits, and patients of unknown sex for 193 visits. Among the 63,539 psychotropic drugs items, the male patients accounted for 26,807 (42.2%) items, the female patients for 36,485 (57.4%) items, and patients of unknown sex for 247 items. Figure 1 shows the distribution of psychotropic drug prescriptions for male and female patients at different ages. Significant effect of gender

**Table 3. Distribution of psychotropic drug prescriptions by age**

| Age groups | No. of all visits | Visit with psychotropic drug prescriptions | | Psychotropic drug items | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| 0-4 | 62130 | 910 | 1.5 | 934 | 1.5 |
| 5-9 | 45722 | 777 | 1.7 | 814 | 1.8 |
| 10-14 | 23534 | 499 | 2.1 | 571 | 2.4 |
| 15-24 | 51981 | 2391 | 4.6 | 3171 | 6.1 |
| 25-34 | 61911 | 4454 | 7.2 | 6482 | 10.5 |
| 35-44 | 69761 | 7387 | 10.6 | 10688 | 15.3 |
| 45-54 | 64882 | 8384 | 12.9 | 11577 | 17.8 |
| 55-64 | 53117 | 7962 | 15.0 | 10532 | 19.8 |
| 65-74 | 58555 | 9057 | 15.5 | 11523 | 19.7 |
| 75-84 | 30089 | 4958 | 16.5 | 6234 | 20.7 |
| 85- | 5011 | 819 | 16.3 | 1013 | 20.2 |
| All | 526693 | 47598 | 9.0 | 63539 | 12.1 |

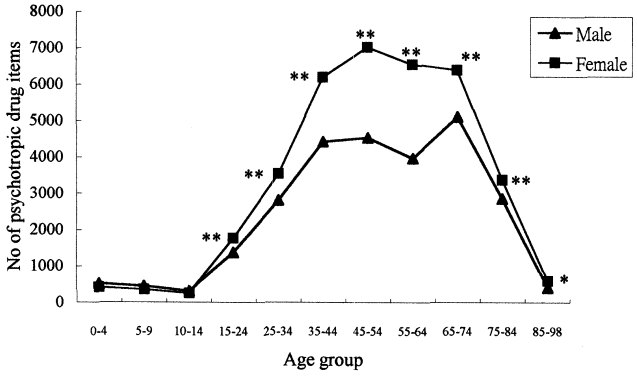


**Fig. 1.** The distribution of psychotropic drug prescriptions for male and female patients at different ages.** $p < 0.001$, * $p < 0.01$

($F = 384.2$, $p < 0.001$) and gender by age interaction ($F = 55.5$, $p < 0.001$) on psychotropic drug prescriptions were observed, indicating that in general greater psychotropic drugs use was found in female than male patients. While no differences between gender was found before age 15, the female patients after late adolescence (age 15 - 98 years) consumed more psychotropic drugs than the male patients ($t = 3.1$ - 22.0, $p < 0.001$) and the differences reached the peak at the age of 45 to 64 years.

## Distribution of psychotropic drug prescriptions by physician's specialty

Table 4 shows the distribution of psychotropic drug prescriptions stratified by physician's specialty. The top 5 specialties (psychiatry, internal medicine, practitioner [physician without specialist title], family medicine, and neurology) contributed to 70.2% of all psychotropic drug items. Among them, albeit only 18.5% (11,766/63,539) items of psychotropic drugs came from psychiatrists, the frequency of prescribing psychotropic drugs was still far higher in psychiatric consultations (87.3% [4,543/5,204]) than in other specialties; followed in order of rankings by the neurologists (45.0% [3,483/7,748]) and the neurosurgeons (30.4% [597/1,967]). It deserves to mention that the cardiologists accounted 26.9% (2,317/8,608) and the gastroenterologists accounted 17.5% (1,383/7,913).

## Distribution of psychotropic drug prescriptions by the status of medical care facilities

Table 5 demonstrated that physicians at the primary care units prescribed 40.4% (25,636/63,539) of psychotropic drug items among all medical facilities. In contrast to that, the frequency of prescribing psychotropic drugs for the visit at the primary care units was much lower (6.15% [20,904/345,497]) compared with 13.5% (9,550/70,976) at the local hospitals, 15.5% (9,028/58,171) at the regional hospitals, and 15.6% (8,116/51,895) at the medical centers, indicating that physicians at the level of medical care facilities above the primary care sector have more chance to prescribe psychotropic drugs in each visit.

**Table 4. Distribution of psychotropic drug prescriptions by physician's specialty (selected 20 specialties in descending order of visit counts)**

| Specialty[a] | No. of all visits | Visit with psychotropic drug prescriptions | | Psychotropic drug items | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| Practitioner[b] | 115739 | 8943 | 7.7 | 10594 | 9.2 |
| Internal Medicine | 64643 | 9064 | 14.0 | 11077 | 17.1 |
| Otorhinolaryngology | 60137 | 2628 | 4.4 | 2817 | 4.7 |
| Family Medicine | 54209 | 4819 | 8.9 | 5858 | 10.8 |
| Pediatrics | 46702 | 1007 | 2.2 | 1129 | 2.4 |
| Gynecology | 36088 | 922 | 2.6 | 1009 | 2.8 |
| Ophthalmology | 30036 | 263 | 0.9 | 275 | 0.9 |
| Dermatology | 20300 | 766 | 3.8 | 818 | 4.0 |
| Surgery | 19119 | 1284 | 6.7 | 1462 | 7.6 |
| Orthopedics | 14099 | 1767 | 12.5 | 1897 | 13.5 |
| Cardiology | 8608 | 2317 | 26.9 | 2715 | 31.5 |
| Gastroenterology | 7913 | 1383 | 17.5 | 1603 | 20.3 |
| Neurorology | 7748 | 3483 | 45.0 | 5293 | 68.3 |
| Rehabilitation | 7510 | 574 | 7.6 | 664 | 8.8 |
| Urology | 5618 | 824 | 14.7 | 940 | 16.7 |
| Psychiatry | 5204 | 4543 | 87.3 | 11766 | 226.1 |
| Endocrinology | 4745 | 605 | 12.8 | 705 | 14.9 |
| Chest Medicine | 3240 | 436 | 13.5 | 487 | 15.0 |
| Nephrology | 2277 | 310 | 13.6 | 371 | 16.3 |
| Neurosurgery | 1967 | 597 | 30.4 | 759 | 38.6 |
| Others | 10791 | 1063 | 9.9 | 1300 | 12.0 |
| All | 526693 | 47598 | 9.0 | 63539 | 12.1 |

[a] The classification of specialties and subspecialties was set by the Bureau of National Health Insurance.
[b] Practitioners here meant physicians without any specialist title specified at claims.

**Table 5. Distribution of psychotropic drug prescriptions by status of medical care facilities**

| Status of medical care facilities | No. of all visits | Visit with psychotropic drug prescriptions | | Psychotropic drug items | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| Medical center | 51895 | 8116 | 15.6 | 11554 | 22.3 |
| Regional hospital | 58171 | 9028 | 15.5 | 13481 | 23.2 |
| Local hospital | 70976 | 9550 | 13.5 | 12868 | 18.1 |
| Primary care unit | 345497 | 20904 | 6.1 | 25636 | 7.4 |
| Others | 154 | - | - | - | - |
| All | 526693 | 47598 | 9.0 | 63539 | 12.1 |

## Distribution of psychotropic drug prescriptions by ATC 3rd level

Totally, 704 kinds of psychotropic drugs appeared in the dataset. They belonged to 73 chemical subgroups of ATC 5th level plus 4 combinations. Table 6 shows the distribution of psychotropic drug prescriptions stratified by drug class of ATC 3rd level. Not only the number of prescription items and their total DDDs were displayed, but also the data were divided into those prescribed by psychiatrists and by other physicians. Besides, the data were extrapolated to the whole population in Taiwan and the numbers of DDDs per 1000 inhabitants per day in each drug group were listed. The average number of DDDs in a psychotropic drug item prescribed by the psychiatrists

Table 6.

was larger than that by the non-psychiatrists (16.8 [197,625/11,766] *vs*. 6.15 [318,362/51,773]) and the differences existed in most drug groups except N06C and N03A. Although only 18.5% (11,766/63,539) of psychotropic drug items were prescribed by the psychiatrists, these prescriptions made up 38.3% (197,625/515,987) of the total DDDs, suggesting that psychiatrist prescribed much lower psychotropic drug items but with higher DDDs, especially for antipsychotics and antidepressants. In that, the psychiatrists played a dominant role in the prescriptions of these two drugs (85.6% of total DDDs in N05A and 65.5% in N06A), whereas non-psychiatrists prescribed 81.9% of total DDDs in anxiolytics (N05B).

The number of DDDs per 1,000 inhabitants per day was estimated to be 32.9 for all kinds of psychotropic drugs, implying 32.9 persons per 1,000 using psychotropic medications. While anxiolytics had 14.3 and hypnotics and sedatives had 10.6 DDDs per 1000 inhabitants per day, antipsychotics and antidepressants had only 3.41 and 3.06 respectively, indicating that among 1,000 people about 25 persons used minor tranqulizers, only 3.4 persons used antipsychotics, 3.06 persons used antidepressants, and 1.2 persons used mood stabilizers.

## Distribution of psychotropic drug prescriptions by ATC 4th and 5th level

At the ATC 4th level, benzodiazepines (N05BA, N05CD, N05CF and N03AE) were the most frequently prescribed drug (69.2% [43,891/63,539] items and 73.5% [379,424/515,987] of DDDs) and had 24.2 DDDs per 1000 inhabitants per day. Antipsychotic drugs were divided into typical and atypical categories. Typical antipsychotics were phenothiazines (N05AA, N05AB, N05AC), butyrophenone (N05AD), thioxanthine (N05AF), benzamides (N05AL) and others (N05AG, N05AH, N05AX); atypical antipsychotics were clozapine and olanzapine (N05AH), and risperdione and zotepine (N05AX). Typicals were 12% of the whole prescribed drug items while atypicals were only 0.7%. Lithium (N05AN) was 4% and other mood stabilizers (N03A, cabamazepine and valporic acid) were 2.7%. Regarding antidepressants, the rate of prescribed

drug items for non-selective monoamine reuptake inhibitors (N06AA, e.g., tricyclic antidepressants) were 3.3%, selective serotonin reuptake inhibitors (N06AB) were 1.8%, monoamine oxidase type A inhibitors (N06AC) was 0.5%, other antidepressants (N06AX trazodone, and venlafaxine) were 2.8% and centrally acting sympathomimetics (N06BA, e.g., methylphenidate) were 0.1%.

Table 7a-e further shows a breakdown by ATC 5th level of psychotropic drugs. Ordered by total DDDs of chemical substance (ATC 5th level) per 1000 inhabitants per day, the top 10 most frequently used psychotropic drugs (Table 7b and 7c) were flunitrazepam (3.40), alprazolam (3.33), fludiazepam(2.53), oxazolam (2.25), lorazepam (2.17), diazepam (1.66), zolpidem (1.65), estazolam (1.49), zopiclone (1.29), and haloperidol (1.08). Besides, introduction of atypical antipsychotics to Taiwan just recently resulted in lower DDDs per 1000 inhabitant per day as compared with the typicals, which had been prescribed for years. On the rank list (Table 7a), haloperidol and sulpiride (0.89) were the top two, while risperdione (0.19), clozapine (0.09), olanzapine (0.04) and zotepine (0.008) ranked the 4th, 9th, 13rd and 17th, respectively. Following the highest DDDs of benzodiazepines, selective serotonin reuptake inhibitor (SSRI) had 1.51 DDDs per 1000 inhabitants per day. Among antidepressants, fluoxetine ranked the first of DDDs (0.73), followed by imipramine (0.43), meclobemide (0.35), trazodone (0.35), and the other SSRIs (paroxetine 0.31, sertraline 0.26, fluoxamine 0.13 and citralopram 0.08 and venlafexaine 0.07) (Table 7d). Albeit carbamazepine, valporic acid and clonazepam (Table 7e) were classified as antiepileptics, they were used as mood stabilizers or anxiolytics (clonazepam) in psychiatric practice. The DDDs for them were 0.76, 0.32 and 0.22 respectively. Another mood stabilizer, lithium (DDDs: 0.13), was categorized in antipsychotics.

### The top 20 brands of the psychotropic drugs marked in Taiwan

Table 8 lists the common psychotropic drugs used in Taiwan (confined to the NHI outpatient sector only). Xanax® was by far the most common one. Among the drugs with ingredient of alprazolam, Xanax® had also the largest market share (81.7% [42,557/52,086 DDDs]). Three flunitrazepams (Modipanol®, Rohypnol®, Flunepan®), three fludiazepam (Erispan®, Era®, Flupine®) and two oxazolam (Serenal®, Secorin®) were also in the ranking list.

## Discussion

To the best of our knowledge, there were some reports[16,17] but no data using the files from BNHI to describe the pattern of psychotropic drug utilization in Taiwan. Although the official statistics released by the Department of Health and BNHI include the yearly expenditure for each therapeutic group of pharmaceutical benefits, detailed information about subgroups of drugs has not been available. The NHI does have its own drug classification system following the structure of the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification. However, the immanent features of the AHFS system limit choices of prescribing measurements and thus hinder international comparisons. The adoption of internationally recognized ATC/DDD system has just been planned within the BNHI. Our study might be the first analysis in standardized measures of ATC/DDD about the pharmacoepidemiology of psychotropic drugs in Taiwan.

Several major observations were derived from this analysis. First, major consumers of psychotropic drugs were between age of 35 - 74 years of age and were more women than men. These findings are consistent with the prevalence of mental illness, especially for anxiety, depression and insomnia across life span and by gender reported in Taiwan[7,18,19] and world-wide.[20-22] Old patients were also found more likely to get psychotropic drugs but with fewer drug items. As the elderly population has increased over the past couple of decades in Taiwan, their mental problems such as sleep disturbance, depression, dementia with behavioral problems should be cautioned. Second, although primary care units consumed 40% of psychotropic drugs, other medical care facilities had higher frequency of psychotropic prescription per

Table 7a.

Table 7b.

Table 7c.

Table 7d.

Table 7e.

**Table 8. The most frequently prescribed brands of psychotropic drugs (top 20 in descending order of total DDD numbers)**

| Brand name[a] | Ingredient | No of prescription items | No of total DDDs |
|---|---|---|---|
| Xanax® | Alprazolam | 3194 | 42557 |
| Stilnox® | Zolpidem | 1413 | 25844 |
| Erispan® | Fludiazepam | 2195 | 21555 |
| Eurodin® | Estazolam | 1528 | 20552 |
| Ativan® | Lorazepam | 2904 | 19898 |
| Imovane® | Zopiclone | 1006 | 19731 |
| Modipanol® | Flunitrazepam | 383 | 18756 |
| Rohypnol® | Flunitrazepam | 518 | 16390 |
| Serenal® | Oxazolam | 1481 | 14935 |
| Loramet® | Lormetazepam | 581 | 11950 |
| Era® | Fludiazepam | 1057 | 9935 |
| Tegretol® | Carbamazepine | 945 | 9712 |
| Halcion® | Triazolam | 504 | 9408 |
| Lexotan® | Bromazepam | 1488 | 9313 |
| Flunepan® | Flunitrazepam | 223 | 8497 |
| Secorin® | Oxazolam | 1286 | 8359 |
| Flupine® | Fludiazepam | 692 | 8104 |
| Valium® | Diazepam | 1749 | 7628 |
| Prozac® | Fluoxetine | 311 | 7163 |
| Serenace® | Haloperidol | 110 | 6611 |

[a] A brand name might include several kinds of drug items with identical component, but in different strengths, forms, or manufacturing countries. For example, Xanax® had 6 different NHI drug codes (0.5 mg tablet [import], 0.5 mg tablet [domestic], 0.25 mg tablet [import], 0.25 mg tablet [domestic], 1 mg extended-release tablet, and 0.5 mg extended-release tablet). DDD = defined daily dose

visit. The ratio of drug prescription was 3-fold greater in the latter ones than the former. The more psychotropic prescriptions with medical facilities of higher level, which take care of more difficult medical problems, indicates that physical disabilities may result in more psychological symptoms. Third, beside psychiatrists to prescribe psychotroipic drugs, prescriptions that contained psychotropic drugs were frequently seen in other major specialties each as neurologists (almost 50%), neurosurgeons (30%), cardiologists (25%) and gastroenterologists (17%). Whether it was related to morbidity spectrums or prescribing habits in these specialties remained unknown. On the contrary, high percentage (87%) of prescribing psychotropic drugs in psychiatric visits might reflect a paradigm shift from psychological approach to pharmacological treatment of mental disorders, given the fact of rapid progress in neuropsychopharmacology.

Our descriptive analysis had some revealing findings. First of all, the usage level of psychotropic drugs in Taiwan, expressed in DDDs per 1000 inhabitants per day, was lower than in most industrialized countries.[23,24] For example, the United States had 26.49 and Japan had 20.71 DDDs for anxiolytics while Taiwan had 14.30 at the outpatient sector. Japan had 39.78 and Australia had 18.19 DDDs /1000 inhabitants/day for hypnotics and sedatives, while Taiwan had 10.64 and the United States had 9.51. The discrepancy was even larger for psychoanaleptics, especially for antidepressants.[25-27] While Australia had 37.7[25] and Sweden had 39.0 DDDs for antidepressants in 1998, Taiwan had 3.06 only and was the lowest among many countries.[24] The age structure and disease prevalence among countries could partly explain the differences.[28-30] And also There was also a particular reason to account for. To avoid rapid increase in budget of the BNHI in Taiwan, the first time to prescribe selective serotonin reuptake inhibitors (SSRIs) was restricted to the psychiatrists only. Additionally, the following refills required approval from the psychiatrists at 6-month intervals. No matter for safety warranty for patients or financial concerns of the BNHI, such prescribing limitation would have discouraged the antidepressant use. Beside that, much less use of antidepressants in Taiwan might be attributed to underdiagnosis of depression.

It is not unique to Taiwan that most of the psychotropic drugs were not prescribed by the psychiatrists.[31] Although psychiatrists prescribed most of antipsychotics and antidepressants, 80% of the main prescriptions (anxiolytics or hypnotics) of the psychotropic drugs were given by non-psychiatrists. Despite that, psychiatrists prescribed about 3-fold greater DDDs/1000 inhabitants/day than non-psychiatrists, reflecting more drug items given in each psychiatric visit. We also found high ratio of anxiolytics to antidepressants use in Taiwan, which is in contrast to equal consumption of both drugs in many developed countries.[24] Rapid promotion of SSRI antidepressants, given the efficacy on the increased rate of depression, and more strict control of benzodiazepines

use to avoid drug dependence may count. In addition, antipsychotics administrated in Taiwan were mainly haloperidol and sulpiride. Only 10% of antipsychotics were of atypicals, which had not been introduced to Taiwan until recently.

Among the top 10 psychotropic substances, the top 9 drug items were of anxiolytics or hypnotics. The top 2 chemical subgroups of drugs (flunitrazepam and alprazolam) accounted for 20.43% (105,392/515,987 DDDs) of all psychotropic drug use in Taiwan. The greater use of both drugs aroused concern about the problems of potential drug dependence. The DDDs for flunitrazepam set by WHO was 1 mg and differed from the prescribing habit with daily quantity of 2 mg in Taiwan. Even after dividing by 2, the number of DDDs (20.15 [(53,306/1,323)/2]) for prescription of flunitrazepam was still high. Although a special law to control addictive substances has been implemented in Taiwan, the BNHI should also pay attention to utilization of psychotropic drugs by the insured.

There were several drawbacks in our study. First, as the datasets arose from a cross-sectional visit-based sampling, the longitudinal data of individual patients, required for dynamic analysis across time, were not available. A dataset of 5-year (1996-2000) longitudinal data from 50,000 sampled people was announced by the NHIRD to be released in 2002. It would then become possible to compare the rate of psychotropic drug exposure with available epidemiological data of mental illnesses in Taiwan. Second, before 1999, the primary care units were exempted from submitting prescription data if the daily drug fee as a lump sum of the prescriptions within three days was charged. Therefore, a trend analysis for individual patients over a longer period would not be completely feasible in the near future. Third, our analysis avoided mentioning diagnoses, which is the key factor to determine use of psychotropic drugs. The diagnoses of the claims in the insurance system notoriously serve for the purpose of reimbursement only and are rarely verified, especially in the outpatient sector. While the traditional methodology for psychiatric epidemiological study cannot be replaced for prevalence determination, the new field of pharmacoepidemiology falls within or is supplementary to epidemiology.[32] The drug utilization analysis in large scale alone should be able to provide information with its unique nature. Fourth, although private prescriptions, which were only few and dispensed at independent practicing pharmacies and were not included in this NHI datasets for analysis, the current results would not have big difference as the NHI covers almost the total drug dispenses in Taiwan. However, what we need to concern is the patients' compliance to the psychotropic medications, which has yet remained unknown.

In the era of computerized prescripting,[33] the insurance claims database, serving as the convenient and efficient data sources, will be invaluable to health care researchers of all specialties[34] and for making appropriate policy to promote health of individuals and the society. The goals in the near future are to focus on the analysis of general trend for each psychotropic substance across time and to associate the pharmacoepidemiological data in parallel with the upcoming epidemiological study of mental disorders in Taiwan.

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