

A cross-sectional study on the drug usage of insomnia in the Chinese medicine hospital in Longgang, Shenzhen

Jingfeng Lin

Hangzhou Seventh Peoples Hospital

Zhenyi Wang

Beijing University of Chinese Medicine

Danfeng Tian

Beijing University of Chinese Medicine

Run Xi

Shenzhen Hospital of Beijing University of Chinese Medicine (Longgang)

Lina Zhang

Hangzhou Seventh Peoples Hospital

Zhenyun Han (✉ tohanzhenyun@sina.com)

Shenzhen Hospital of Beijing University of Chinese Medicine (Longgang)

Research Article

Keywords: Shenzhen, insomnia, drug usage

Posted Date: February 3rd, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1214359/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Introduction

Insomnia was widely distributed among the population, and it was a risk factor for many diseases. To evaluate the condition of usage of drugs in Chinese hospital of Longgang, Shenzhen, we carried this cross-sectional research. We extracted the information of drug usage, symptoms of patients by R software (version 4.0.2) from Hospital Information System (HIS). The research was registered in Chinese Clinical Trial Registry, ChiCTR2000040703.

Methods

A retrospective, cross-sectional study was conducted in Shenzhen Hospital of Beijing University of Chinese Medicine (Long Gang). Insomnia patients from Jan 1, 2016 to Nov 10, 2020 were included to cross-sectional study. We analyzed the basic information, the condition of drug usage and the relation of symptoms and drug usage by R software (version 4.0.2).

Results

Totally 9439 patients were included in the study. The average age of these patients was 45.81years (SD 13.97 years). Anxiety, dreaminess, dizzy, palpitation, headache, thirsty, weakness, chest distress, annoyance, abdominal distension, bad moods, difficulty falling asleep and bitter taste were core symptoms of insomnia. Totally 14256 times (67.65%) patients received drug prescription and more than one insomnia drug was administered in 8355 patients. The 10 most used drugs ranged from more to less were Estazolam (29.99%), Zaoren Anshen Capsule (15.50%), Oryzanol (14.82%), Diazepam (14.51%), Flupentixol and Melitracen (14.30%), Alprazolam (8.12%), Zolpidem Tartrate (5.29%), Vitamin B6 (4.76%), Sertraline (4.03%), Clonazepam (2.97%).

Conclusion

The drug usage for insomnia in the Chinese medicine hospital in Long gang, Shenzhen were mainly included benzodiazepines, nonbenzodiazepines, Chinese patent medicines, anti-anxiety and anti-depression drugs, Oryzanol and Vitamin B6. The usage of Oryzanol and Vitamin B6 should be abused in Chinese medicine hospital, and the usage of Chinese medicine should be more rigorously evaluated. The nonbenzodiazepines should be promoted and broader understood in Chinese medicine hospital in Longgang, Shenzhen.

1. Introduction

Insomnia is broadly defined as dissatisfaction with sleep either qualitatively or quantitatively[1]. The rates of insomnia varied from 6%-19%[2, 3]. Classical benzodiazepines and benzodiazepine receptor agonists (BZRAs, Nonbenzodiazepines; Zopiclone, Zolpidem, and Zaleplon) are used in managing insomnia, but antidepressants are also used in clinical practice, although there is less evidence of their efficacy[4]. In

additional, antipsychotics, antihistamines, phytotherapeutic substances and melatonin were also used as the therapeutic regimen for insomnia with lower evidence[2]. Insomnia could be a risk factor for cardiovascular diseases[5-7], arterial hypertension, myocardial infarction, chronic heart failure[8, 9], type 2 diabetes[10] and obesity and hypertension[11]. So, a big data analysis on the drug usage of insomnia was very necessary to help evaluating the rationality of drug usage. In China, to evaluate the condition of usage of drugs in Longgang Shenzhen, we carried this cross-sectional research. We extracted the information of drug usage, symptoms of patients by R software (version 4.0.2) from Hospital Information System (HIS). The association rules analysis was carried to find out the relationship with symptoms and the usage of drugs. The research was registered in Chinese Clinical Trial Registry, ChiCTR2000040703.

2. Methods

2.1 Study setting and patients

A retrospective, cross-sectional study was conducted in Shenzhen Hospital of Beijing University of Chinese Medicine (Long Gang). Insomnia patients from Jan 1, 2016 to Nov 10, 2020 were included to cross-sectional study. The included criteria were: (1) International Classification of Sleep Disorders (ICSD-3) Diagnostic Criteria for short-term and chronic insomnia. (2) We excluded patients that were of mental or nervous system dysfunction, or unable to express willingness. This study was approved by the ethics committee of Shenzhen Hospital of Beijing University of Chinese Medicine (Long Gang).

2.2 Data collection and analysis

The information of patient, medication, and microbiologic examination, including register number, age, sex, diagnosis, admission time were collected from Shenzhen Hospital of Beijing University of Chinese Medicine Hospital Information System (HIS) by clinical practitioners. Data were analyzed by R software (version 4.0.2).

3. Results

3.1 Baseline patient characteristics

Totally 9439 patients were included in the study, with 21073 times coming to the doctors, among who 3470 (39.6%) were male, and 5699 (60.4%) were female. With there were 6577 patients (69.7%) and 14256 (67.7%) times coming included in the retrospective cross-sectional study to assess the drug use. The average age of these patients was 45.81years (SD 13.97 years). Table 1 shows the characteristics of 9439 included patients.

Table 1: The characteristics of 9439 included patients

	All	Male	female	P-value
Average age				
Mean (SD)	45.81 (±13.97)	45.28 (±13.92)	46.16 (±14.00)	0.001
Agegroup				
≤30	1154 (12.23%)	456 (39.51%)	698 (60.49%)	0.0005
31-45	3740 (39.63%)	1573 (42.06%)	2167 (57.94%)	
46-60	3050 (32.32%)	1164 (38.16%)	1886 (61.84%)	
>60	1493 (15.82%)	547 (36.64%)	946 (63.36%)	

*Excluded the patients with no information of age

3.2 Use of benzodiazepine

Table 2: Use of benzodiazepine

Drugs	Frequency	Rates
Estazolam	4276	29.99%
Diazepam	2069	14.51%
Alprazolam	1157	8.12%
Clonazepam	424	2.97%

Among the total of 21073 times, 14256 times (67.65%) patients received drug prescription and more than one insomnia drug was administered in 8355 patients. Among the patients using with benzodiazepines, 4276(29.99%) patients received estazolam, 1157(8.12%) patients received Alprazolam, 2069(14.51%) patients received Diazepam. Among the 754(5.29%) patients received Zolpidem Tartrate, 424(2.97%) patients received Clonazepam (Table 2).

3.3 Use of nonbenzodiazepine

Table 3: Use of nonbenzodiazepine

Drugs	Frequency	Rates
Zolpidem Tartrate	754	5.29%
Dexzopiclone	119	0.83%

Among the patients using with nonbenzodiazepines, 754(5.29%) patients received Zolpidem Tartrate, 119(0.83%) patients received Dexzopiclone (Table 3).

3.4 Use of Chinese patent medicines

Table 4: Use of Chinese patent medicines

Drugs	Frequency	Rates
Zaoren Anshen Capsule	2209	15.50%
Shumian Capsule	400	2.81%

Totally 2209(15.50%) patients received Zaoren Anshen Capsule and 400 (2.81%) patients received Shumian Capsule (Table 4).

3.5 Use of traditional Chinese medicines

Among 4406(30.91%) comings used traditional Chinese medicines.

3.6 Use of anti-anxiety and anti-depressants

Among the all patients, 2038 (14.3%) were given Flupentixol and Melitracen. And of the 575(4.03%) patients took Sertraline (Table 5).

Table 5: Use of anti-anxiety and anti-depressants

Drugs	Frequency	Rates
Flupentixol and Melitracen	2038	14.30%
Sertraline	575	4.03%
Escitalopram	120	0.84%

3.7 Use of other kinds of medicine

Among the all patients, 2113 (14.82%) were given Oryzanol. And of the 679 (4.76%) patients took Vitamin B6 (Table 6).

Table 6: Other kinds of medicine

Drugs	Frequency	Rates
Oryzanol	2113	14.82%
vitamin B6	679	4.76%

3.8 Symptoms collection

A total of 17,337 outpatient electronic medical records (EMRs) were obtained by screening the included patient, and the retention of EMRs accounted for 82.27% of the total number of patients. The R software stringr package was used to extract the symptoms and signs information contained in the medical records. The extracted symptom and sign information results were sorted in descending order. The top 20 symptoms were selected, and the results were as follows:

Table 7: Top 20 symptoms of insomnia

Symptoms	Freq	Rates
Anxiety	3803	21.94%
Dreaminess	2883	16.63%
Dizzy	2063	11.90%
Palpitation	1985	11.45%
Headache	1867	10.77%
Upset	1694	9.77%
Thirsty	1681	9.70%
Weakness	1659	9.57%
Chest distress	1538	8.87%
Annoyance	1143	6.59%
Abdominal distension	1138	6.56%
Difficulty falling asleep	1123	6.48%
Bitter taste	1108	6.39%
Bad moods	978	5.64%
Constipation	464	2.68%
Soreness of waist	443	2.56%
Eat less	365	2.11%
Lambago	272	1.57%
Loose stool	212	1.22%
Tinnitus	189	1.09%
Short of breath	148	0.85%
Dry throat	134	0.77%
Irritable	125	0.72%
Early awaking	118	0.68%
Idrosis	101	0.58%

From Table 7, we could conclude that anxiety, dreaminess, dizzy, palpitation, headache, thirsty, weakness, chest distress, annoyance, abdominal distension, bad moods, difficulty falling asleep and bitter taste were core syndromes of insomnia.

3.9 Reinteraction of symptoms and drugs

We select the patients using benzodiazepine, nonbenzodiazepine, Chinese patent medicines, oryzanol and vitamin B6 respectively, anti-anxiety and anti-depressants and summary the times of syndromes appearing in the patients. The results were as following (Table 8):

Table 8: Different kinds of drugs and its main symptoms

Kinds of drugs	Symptoms	Freq	Rates
Benzodiazepine			
	Anxiety	2310	31.35%
	Dreaminess	1030	13.98%
	Palpitation	611	8.29%
	Dizzy	572	7.76%
	Upset	527	7.15%
	Headache	513	6.96%
	Weakness	498	6.76%
	Chest distress	482	6.54%
	Difficulty falling asleep	408	5.54%
	Dry throat	392	5.32%
Nonbenzodiazepine			
	Anxiety	187	21.59%
	Dreaminess	105	12.12%
	Difficulty falling asleep	95	10.97%
	Palpitation	88	10.16%
	Headache	84	9.70%
	Upset	78	9.01%
	Dizzy	78	9.01%
	Chest distress	73	8.43%
	Weakness	72	8.31%
	Abdominal distention	60	6.93%
Chinese patent medicines			
	Dreaminess	355	20.89%
	Palpitation	279	16.42%
	Anxiety	261	15.36%
	Dizzy	205	12.07%
	Abdominal distention	195	11.48%

Headache	194	11.42%
Chest distress	174	10.24%
Weakness	156	9.18%
Dry throat	126	7.42%
Upset	120	7.06%
Oryzanol and vitamin B6		
Anxiety	1192	52.74%
Dreaminess	728	32.21%
Upset	192	8.50%
Headache	151	6.68%
Dizzy	104	4.60%
Bad moods	103	4.56%
Weakness	97	4.29%
Bitter taste	87	3.85%
Dry throat	75	3.32%
Difficulty falling asleep	74	3.27%
Anti-anxiety and anti-depressants		
Anxiety	1466	60.06%
Dreaminess	564	23.11%
Bad moods	539	22.08%
Upset	376	15.40%
Dizzy	205	8.40%
Difficulty falling asleep	200	8.19%
Headache	176	7.21%
Palpitation	172	7.05%
Weakness	140	5.74%
Dry throat	103	4.22%

For the patients who received benzodiazepine, nonbenzodiazepine, Oryzanol and vitaminB6, and Anxiety and depression, most common symptom was Anxiety. However, for Chinese patent medicines, most

common symptom was Dreaminess.

Association rules analysis was carried for various symptoms and different kinds of drugs by arules package, R software. In the analysis of association rules of kinds of drugs and symptoms, we selected association rules of support degree >0.01 and confidence degree >0.1 to find the association rules between benzodiazepine and symptoms, and we selected association rules of support degree >0.005 and confidence degree >0.05 to find the association rules between Chinese patent medicines, Oryzanol and Vitamin, Anti-anxiety and anti-depressants and symptoms. We also found that there were no significant association rules between Nonbenzodiazepines and symptoms. The aruleViz package was used to draw the correlation diagram, and the results were shown in Figure 1.

Figure 1: Association rules analysis of drug usage and symptoms

The results showed that patients received benzodiazepines were associated with Anxiety, Dreaminess, Upset, Bitter taste, Difficulty falling asleep, Chest distress, Palpitation, Weakness, Headache, Dizzy, Thirsty, Abdominal distension, which were in accordance with the result in Table. Patients received Chinese patent medicines were associated with Dizzy, Weakness, Dreaminess, palpitation, chest distress and headache. Patients received Oryzanol and Vitamin were associated with Headache, anxiety, dreaminess and upset. Patients received anti-anxiety or anti-depression drugs were associated with anxiety, bad mood, upset, dizzy, dreaminess and headache.

4. Discussion

This study evaluates the drug use in treating the patients in Longgang, Shenzhen, who suffered from insomnia and recorded by Hospital Information System (HIS) in Shenzhen Hospital of Beijing University of Chinese Medicine(Long Gang). About 9439 patients were included in the study, with 21073 times coming to the doctors to assess the rationality of drug use and the majority of them are female(60.4%). The results demonstrate that benzodiazepine, nonbenzodiazepine, traditional Chinese medicines, Oryzanol and vitaminB6 are the principal drugs to treat insomnia in patients. Anti-anxiety and anti-depression are the main prescript drugs for insomnia combined with the symptoms of anxiety and depression.

In European insomnia guideline, the Benzodiazepines, benzodiazepine receptor agonists and some antidepressants are effective in the short term treatment of insomnia, and phytotherapeutics are not recommended for insomnia treatment[2]. In our research, we found that Chinese patent medicines(18.31%) and traditional Chinese medicines(30.91%) were widely used in Shenzhen Hospital of Beijing University of Chinese Medicine(Long Gang), which was contradicted to the guidelines. In other cross-sectional about drug usage for insomnia, Suzanne M. Bertisch[3] did not reported the significant efficacy of phytotherapeutics in a big cross-sectional research of prescription medications for insomnia in America. Xiaojia Ni[12] made a meta-analysis on efficacy of Chinese medicine on insomnia compared with placebo, and found that the Chinese medicine was better than placebo, however, the quality of included studies was pool[2]. So, we thought the efficacy of Chinese medicine on insomnia and the

rationality of drug use in Shenzhen Hospital of Beijing University of Chinese Medicine(Long Gang) should be further evaluated.

For benzodiazepine and nonbenzodiazepine, a meta-analysis indicated that there were no difference between them[13]. In terms of side effects, both of benzodiazepine and nonbenzodiazepine have the potential for tolerance and dependency. In our research, we found that the usage of benzodiazepine was far more than nonbenzodiazepine, the reason we thought was the benzodiazepines were more acceptable in doctors' conception in Longgang, Shenzhen.

For Oryzanol and vitamin B6, there were about 14.82% patients received Oryzanol and about 4.76% patients received vitamin B6. In past research, there were no significant evidence indicated that Oryzanol could be helpful to insomnia, and it didn't be recommended in guideline[13]. For vitamin B6, Patrick Lemoine[14] found that the combination of melatonin, vitamin B6, and medicinal plants may be beneficial in mild-to-moderate insomnia. However, there were no evidence for vitamin B6 about whether it was effective for insomnia when single-used.

As for anti-anxiety and anti-depressants, in our research, Deanxit (Flupentixol and Melitracen) and sertraline were mostly used in Beijing University of Chinese Medicine(Long Gang). A research from China also reported the Deanxit (Flupentixol and Melitracen) was widely used in 20 national hospitals of China, however, there was no precise evidence manifested the Deanxit (Flupentixol and Melitracen) was effective to insomnia and was not be recommended in guideline[2]. For sertraline, there were some evidence indicated that antidepressant pharmacotherapy could relief the symptoms in patients with comorbid depression and insomnia[15] and the efficiency was exactly[2]. Alexander Winkler[16] made an analysis on antidepressant drugs and found that the efficacy of antidepressants was weaker than that for benzodiazepines and nonbenzodiazepines on insomnia. Other researches indicated that adverse effects and study withdrawals did not significantly differ between participants receiving antidepressants and those receiving placebo[17]. We considered that anti-anxiety and anti-depressants should be specifically used in patients with comorbid depression and insomnia.

For the relationship between symptoms and different kinds of drugs (Fig. 1), we would find that antidepressant and anti-anxiety drugs were related to anxiety, bad moods and dreaminess, while benzodiazepines and Chinese patent medicines were related with much more kinds of symptoms.

For the drug usage of insomnia in Shenzhen, Longgang, we thought that the use of Chinese patent medicine and Chinese medicine should be evaluated more carefully. As it was well known that there were much Chinese medicine and Chinese patent medicine used in Chinese medicine hospital of China. However, the usage of Chinese medicine was lack of proper efficacy evaluation and clinical trial or observation with high level evidence[2]. The more rigorous, high-quality clinical trials should be carried to evaluate the exact efficacy in specific patients.

In additional, we thought the nonbenzodiazepine had some advantages than benzodiazepine and should be promoted in Chinese medicine hospital. Some non-benzodiazepines compared to traditional

benzodiazepines, non-benzodiazepines may have less disruptive of sleep stages, have lesser effects on next day psychomotor performance and be more safety[18, 19].

For the deficiencies of this research, foremost, the data of research was from the HIS, and some clinicians would omit or miswrite some information during the busy work, the data could have some biases and some incompleteness. P. W. Handayani[20] pointed that the HIS still needs to be refined in terms of providing optimal health services in development countries, and there was considerable dissatisfaction with the quality of the existing HIS among doctors. In addition, the information of patients in HIS of Chinese medicine hospital, Longgang, Shenzhen were only containing sex and age, other important information was not recorded. So, as a sectional study, the information collection was inadequate.

In conclusion, the drugs used for insomnia in the Chinese medicine hospital in Longgang, Shenzhen were mainly included benzodiazepine, nonbenzodiazepine, Chinese patent medicines, anti-anxiety and anti-depression drugs, oryzanol and vitamin B6. Oryzanol and vitamin B6 should be abused in Chinese medicine hospital, and the usage of Chinese medicine should be more rigorous evaluated. The nonbenzodiazepine should be promoted and broader understood in Chinese medicine hospital in Longgang, Shenzhen.

Abbreviations

HIS: Hospital Information System; BZRA: Benzodiazepine receptor agonist.

Declarations

Statement of Ethics

The experiment was approved by Ethic committee of Shenzhen Hospital of Beijing university of Chinese medicine. All methods in this research were carried out in accordance with STROBE guideline. Informed consent was obtained from all subjects or their legal guardians.

Availability of data and materials

The data that support the findings of this study are available from authors by emails but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Conflict of Interest Statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Consent for publication

All authors read and approved to publish the final manuscript.

Funding

This work is funded by National Key Research and Development Plan (SQ2019YFC170218).

Acknowledgments

Thanks to Information Department of Shenzhen Hospital of Beijing University of Chinese Medicine (Longgang), who extracted the data for this research from Hospital Information System.

Authors' contributions

Jingfeng Lin, Zhenyi Wang and Danfeng Tian performed the integral research. Jingfeng Lin and Run Xi performed data screen and data analysis. Zhenyun Han and Lina Zhang conceived and supervised the study. Jingfeng Lin, Zhenyi Wang and Danfeng Tian drafted the manuscript.

References

1. Patel D, Steinberg J, Patel P: **Insomnia in the Elderly: A Review**. *J Clin Sleep Med* 2018, **14**(6):1017-1024.
2. Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, Espie CA, Garcia-Borreguero D, Gjerstad M, Goncalves M *et al*: **European guideline for the diagnosis and treatment of insomnia**. *J Sleep Res* 2017, **26**(6):675-700.
3. Bertisch SM, Herzig SJ, Winkelman JW, Buettner C: **National use of prescription medications for insomnia: NHANES 1999-2010**. *Sleep* 2014, **37**(2):343-349.
4. Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, Klassen TP, Witmans M: **The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs**. *J Gen Intern Med* 2007, **22**(9):1335-1350.
5. Li M, Zhang X-W, Hou W-S, Tang Z-Y: **Insomnia and risk of cardiovascular disease: A meta-analysis of cohort studies**. *International Journal of Cardiology* 2014, **176**(3):1044-1047.
6. Sofi F, Cesari F, Casini A, Macchi C, Abbate R, Gensini GF: **Insomnia and risk of cardiovascular disease: a meta-analysis**. *European journal of preventive cardiology* 2014, **21**(1):57-64.
7. Meng L, Zheng Y, Hui R: **The relationship of sleep duration and insomnia to risk of hypertension incidence: a meta-analysis of prospective cohort studies**. *Hypertension Research* 2013, **36**(11):985-995.
8. Palagini L, Maria Bruno R, Gemignani A, Baglioni C, Ghiadoni L, Riemann D: **Sleep loss and hypertension: a systematic review**. *Current pharmaceutical design* 2013, **19**(13):2409-2419.
9. Laugsand LE, Vatten LJ, Platou C, Janszky I: **Insomnia and the risk of acute myocardial infarction: a population study**. *Circulation* 2011, **124**(19):2073-2081.
10. Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A: **Sleep disturbances compared to traditional risk factors for diabetes development: systematic review and meta-analysis**. *Sleep*

medicine reviews 2016, **30**:11-24.

11. Buxton OM, Marcelli E: **Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States.** *Soc Sci Med* 2010, **71**(5):1027-1036.
12. Ni X, Shergis JL, Guo X, Zhang AL, Li Y, Lu C, Xue CC: **Updated clinical evidence of Chinese herbal medicine for insomnia: a systematic review and meta-analysis of randomized controlled trials.** *Sleep Med* 2015, **16**(12):1462-1481.
13. Dündar Y, Dodd S, Strobl J, Boland A, Dickson R, Walley T: **Comparative efficacy of newer hypnotic drugs for the short-term management of insomnia: a systematic review and meta-analysis.** *Human Psychopharmacology: Clinical and Experimental* 2004, **19**(5):305-322.
14. Lemoine P, Bablon J-C, Da Silva C: **A combination of melatonin, vitamin B6 and medicinal plants in the treatment of mild-to-moderate insomnia: A prospective pilot study.** *Complementary Therapies in Medicine* 2019, **45**:104-108.
15. Manber R, Buysse DJ, Edinger J, Krystal A, Luther JF, Wisniewski SR, Trockel M, Kraemer HC, Thase ME: **Efficacy of Cognitive-Behavioral Therapy for Insomnia Combined With Antidepressant Pharmacotherapy in Patients With Comorbid Depression and Insomnia: A Randomized Controlled Trial.** *J Clin Psychiatry* 2016, **77**(10):e1316-e1323.
16. Winkler A, Auer C, Doering BK, Rief W: **Drug Treatment of Primary Insomnia: A Meta-Analysis of Polysomnographic Randomized Controlled Trials.** *CNS Drugs* 2014, **28**(9):799-816.
17. Wilt TJ, MacDonald R, Brasure M, Olson CM, Carlyle M, Fuchs E, Khawaja IS, Diem S, Koffel E, Ouellette J *et al*: **Pharmacologic Treatment of Insomnia Disorder: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians.** *Ann Intern Med* 2016, **165**(2):103-112.
18. Tsai JH, Yang P, Chen CC, Chung W, Tang TC, Wang SY, Liu JK: **Zolpidem-induced amnesia and somnambulism: rare occurrences?** *Eur Neuropsychopharmacol* 2009, **19**(1):74-76.
19. Hassinger AB, Bletnisky N, Dudekula R, El-Solh AA: **Selecting a pharmacotherapy regimen for patients with chronic insomnia.** *Expert Opin Pharmacother* 2020, **21**(9):1035-1043.
20. Handayani PW, Hidayanto AN, Pinem AA, Sandhyaduhita PI, Budi I: **Hospital information system user acceptance factors: User group perspectives.** *Informatics for Health and Social Care* 2017, **43**(1):84-107.

Figures

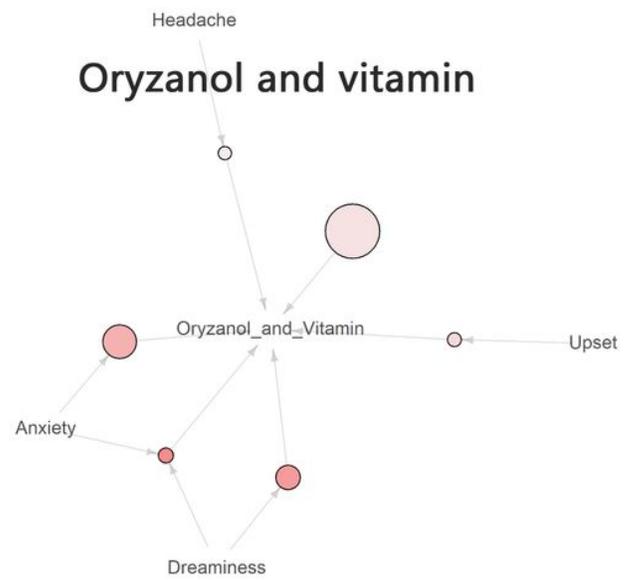
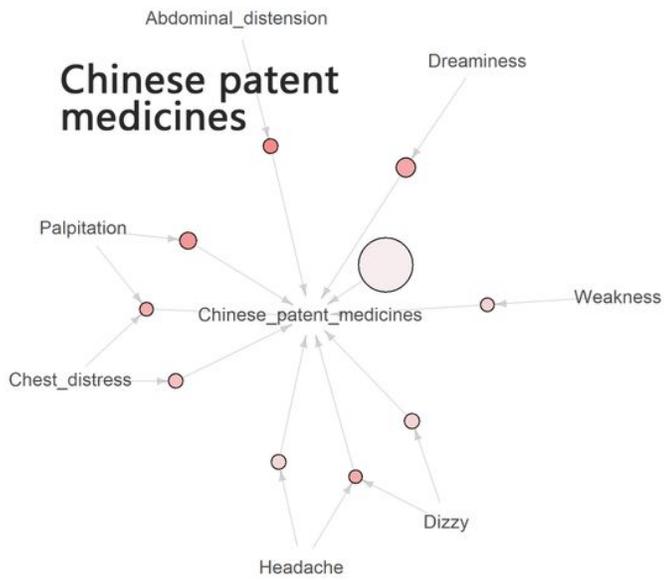
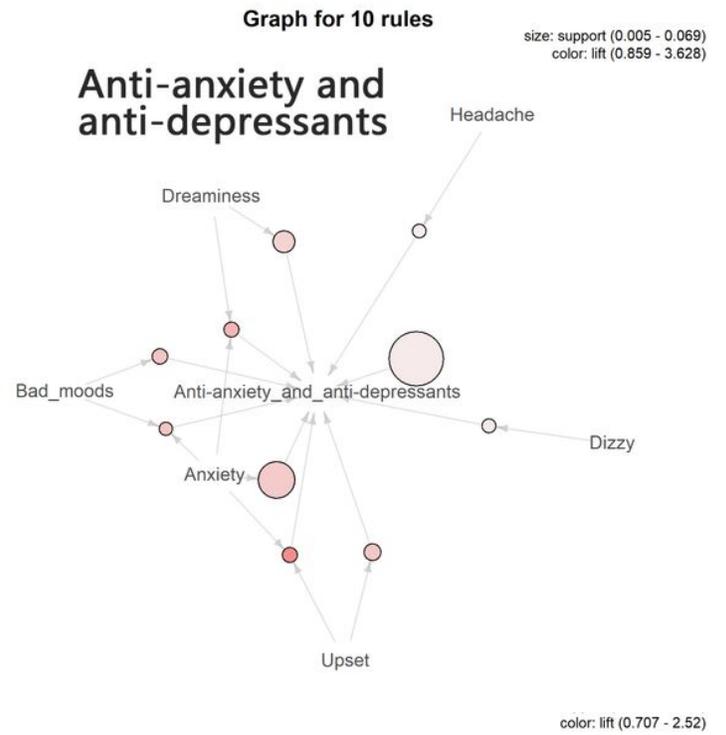
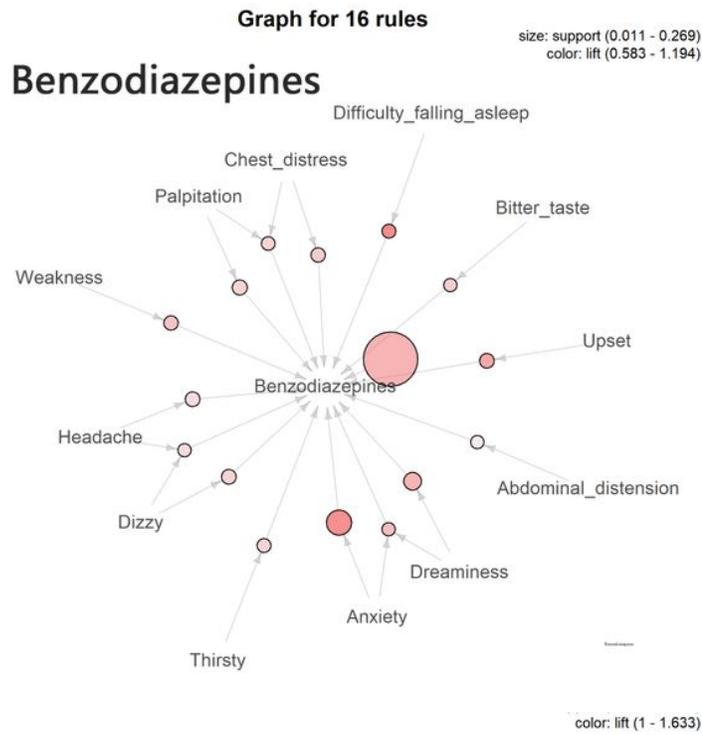


Figure 1

Association rules analysis of drug usage and symptoms