表5　向精神薬のクラス間多剤併用処方のパターン（2002〜2010年）

	抗精神病薬		抗うつ薬（包含）		抗うつ薬（限定）		気分安定薬（包含）		気分安定薬（限定）		ADHD治療薬		抗不安・睡眠薬	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
0〜5歳														
クラス内処方数	27		21		3		215		0		8		83	
クラス間多剤併用	4	14.8	2	9.5	2	66.7	15	7.0	—	—	3	37.5	2	2.4
抗精神病薬	—	—	1	4.8	1	33.3	3	1.4	—	—	3	37.5	1	1.2
抗うつ薬（包含）	1	3.7	—	—	—	—	1	0.5	—	—	0	0.0	2	2.4
抗うつ薬（限定）	1	3.7	—	—	—	—	0	0.0	—	—	0	0.0	2	2.4
気分安定薬（包含）	3	11.1	1	4.8	0	0.0	—	—	—	—	4	50.0	10	12.0
気分安定薬（限定）	0	0.0	0	0.0	0	0.0	—	—	—	—	0	0.0	0	0.0
ADHD治療薬	3	11.1	0	0.0	0	0.0	4	1.9	—	—	—	—	0	0.0
抗不安・睡眠薬	1	3.7	2	9.5	2	66.7	10	4.7	—	—	0	0.0	—	—
6〜12歳														
クラス内処方数	165		487		54		562		3		202		167	
クラス間多剤併用	62	37.6	40	8.2	31	57.4	78	13.9	2	66.7	23	11.4	38	22.8
抗精神病薬	—	—	22	4.5	19	35.2	33	5.9	2	66.7	19	9.4	30	18.0
抗うつ薬（包含）	22	13.3	—	—	—	—	9	1.6	1	33.3	12	5.9	13	7.8
抗うつ薬（限定）	19	11.5	—	—	—	—	7	1.2	1	33.3	6	3.0	12	7.2
気分安定薬（包含）	33	20.0	9	1.8	7	13.0	—	—	—	—	23	11.4	32	19.2
気分安定薬（限定）	2	1.2	1	0.2	1	1.9	—	—	—	—	0	0.0	1	0.6
ADHD治療薬	19	11.5	12	2.5	6	11.1	23	4.1	0	0.0	—	—	1	0.6
抗不安・睡眠薬	30	18.2	13	2.7	12	22.2	32	5.7	1	33.3	1	0.5	—	—
13〜18歳														
クラス内処方数	802		577		480		590		40		63		1,026	
クラス間多剤併用	502	62.6	403	69.8	361	75.2	200	33.9	35	87.5	15	23.8	594	57.9
抗精神病薬	—	—	206	35.7	189	39.4	147	24.9	32	80.0	13	20.6	421	41.0
抗うつ薬（包含）	206	25.7	—	—	—	—	55	9.3	9	22.5	5	7.9	332	32.4
抗うつ薬（限定）	189	23.6	—	—	—	—	43	7.3	6	15.0	4	6.3	298	29.0
気分安定薬（包含）	147	18.3	55	9.5	43	9.0	—	—	—	—	7	11.1	120	11.7
気分安定薬（限定）	32	4.0	9	1.6	6	1.3	—	—	—	—	1	1.6	20	1.9
ADHD治療薬	13	1.6	5	0.9	4	0.8	7	1.2	1	2.5	—	—	1	0.1
抗不安・睡眠薬	421	52.5	332	57.5	298	62.1	120	20.3	20	50.0	1	1.6	—	—

件のうち，11%は包含的定義の気分安定薬，9%は抗精神病薬，6%は包含的定義の抗うつ薬が併用されていた．13〜18歳において抗精神病薬処方のある802件のうち，53%は抗不安・睡眠薬，26%は包含的定義の抗うつ薬が併用されていた．13〜18歳において包含的定義の抗うつ薬処方のある577件のうち，58%は抗不安・睡眠薬，36%は抗精神病薬が併用されていた．

全調査年における向精神薬間の併用禁忌の処方として，sultoprideは6件中2件，thioridazineは9件中1件，pimozideは40件中2件にみられた．併用禁忌処方のあったレセプトの調査年は，2004年以前であった．

Ⅲ．考　　察

本研究では，社会医療診療行為別調査を活用して，子どもに対する向精神薬処方の経年変化を検討した結果，①向精神薬の処方件数が増加していること，②向精神薬のクラス間多剤併用処方は高頻度にみられることが示された．以下に，この2つの主要な結果が得られた要因と今後の課題を考察する．

1．向精神薬の処方件数の増加

本研究では，2002～2010年の9年間で，6～12歳におけるADHD治療薬と抗精神病薬の処方件数が増加していること，13～18歳においてはそれに加え，抗うつ薬の処方件数も増加していることが示された．このような向精神薬の処方件数の増加には，次の3つの要因が寄与していると考えられる．

第1の要因は，精神疾患による未成年の受診者数の増加である．患者調査によると，2002～2008年にかけて未成年の精神疾患による受診者数は増加している．なかでもその増分が最も大きいのが，その他の精神障害（F01，F03，F1，F2，F3，F4，F7以外）であり，次いで気分障害（F30～F39）が36%増，神経性障害など（F40～F48）が15%増と続き，一方，統合失調症（F20～F29）については増減なしという結果が示されている[20,24]．また，未成年に限定できないデータであるものの，その他の精神障害のうち，広汎性発達障害（F84.0，F84.1，F84.5，F84.8，F84.9，F88～F89）が3.7倍増，ADHD（F90）が2倍増という報告もある[21,23]．抗精神病薬や抗うつ薬は，成人で適応のある統合失調症，大うつ病性障害，強迫性障害，社交不安障害ばかりでなく，広汎性発達障害やADHDなどにも使用されていることを踏まえると[33,52]，近年における向精神薬の処方件数増加は，広汎性発達障害やADHDによる受診者数の増加による可能性が推測される．

第2の要因は，子どもの精神疾患に対応できる医師数や医療施設数の増加である．近年わが国では，思春期外来の数は著しく増加しており，2001年に523施設であった思春期外来は，2009年には1,746施設となっている[49]．また，2005年度における厚生労働省主催の「子どもの心の診療医の養成に関する検討会」では，わが国では子どもの心の診療医が少なく，その確保・養成が急務であることが指摘されていたが[28]，その後，関連学会などの努力により子どもの心の診療医の養成が推進されてきた経緯もある．加えて，診療報酬上の評価も医師数と医療施設数の増加に寄与していると考えられる．2002年に20歳未満の患者に対する通院精神療法の加算が新設され，2008年に算定要件が拡大された経緯もあった．こうした経緯により医師数や医療施設数が増加し，向精神薬の処方件数増加に影響を及ぼした可能性も考えられる．

第3の要因は，子どもの精神疾患に対応できる新薬の承認の影響である．2002～2010年の間に，ADHD治療薬として，徐放性methylphenidate（2007年12月販売開始）とatomoxetine（2009年6月販売開始）が上市されている．加えて，新規抗精神病薬として，risperidone内用液（2002年6月販売開始）とaripiprazole（2006年6月販売開始）も上市されている．risperidoneとaripiprazoleは，今後，自閉性障害への適応拡大も期待されている状況がある[22,40]．これらの新規抗精神病薬は子どもに対する適応がないにもかかわらず，すでにカナダにおいては，年々，子どもへの処方件数が増加している現実がある[2]．

2．高頻度のクラス間多剤併用処方

本研究では，向精神薬のクラス間多剤併用処方は，気分安定薬では93%，抗うつ薬では77%，抗不安・睡眠薬では62%，抗精神病薬では61%，ADHD治療薬では17%にみられた．この数値は欧米と比べて著しく高いものである．国際比較研究によると，向精神薬処方を受けた未成年におけるクラス間多剤併用処方の割合は，アメリカ合衆国では19%，オランダ王国では9%，ドイツ連邦共和国では6%であると報告されている[56]．もちろん，この結果をもって，安易に「わが国では，向精神薬の不適切な多剤併用処方の割合が異様に高い」と結論づけるのには慎重であるべきであろう．というのも，国家間の医療提供体制の相違，あるいは，調査対象の等質性を担保できないといった限界を考慮する必要があるからである．とはいえ，今後，わが国の多剤併用処方の割合が欧米よりも高くなる理由について，検討していく必要があるだろう．

本研究ではまた，わが国のクラス間多剤併用処方の内訳が，先行研究とおおむね類似したもので

あることが明らかになった．すなわち，多剤併用処方として，抗精神病薬と抗うつ薬，抗精神病薬と抗不安・睡眠薬，抗うつ薬と抗不安・睡眠薬の組み合わせが高頻度でみられることが示されたのである．先行研究では，抗精神病薬とADHD治療薬[8,48]，抗精神病薬と抗うつ薬[8~10,48]，抗うつ薬とADHD治療薬[8,9,48]，抗うつ薬と抗不安・睡眠薬[10]の組み合わせが高頻度でみられることが報告されており，ADHD治療薬を除いて本研究では先行研究と類似の結果が得られている．

こうした多剤併用処方は，ADHDと不安障害などの併存症例や治療抵抗性の症例への対処の必要性に迫られた結果であると推測される．実際，多剤併用処方の臨床試験は，ADHDとうつ病/不安障害の併存症例へのADHD治療薬と抗うつ薬の併用[1,29]，ADHDと双極性障害の併存症例へのADHD治療薬と抗精神病薬の併用[54]，ADHDにおける治療抵抗性の攻撃性へのADHD治療薬と抗精神病薬[3]や気分安定薬[4]の併用，治療抵抗性の強迫性障害への抗精神病薬と抗うつ薬の併用[30]など，併存症例や治療抵抗性の症例に対処することを想定したデザインで実施されてきた．臨床現場では，こうした臨床試験で想定される患者は決して少なくない現実があり[50]，今回明らかにされたような多剤併用処方が高頻度でみられるという結果につながったと考えられる．

とはいえ，向精神薬のクラス間多剤併用処方の有効性と安全性に関するエビデンスは不足している．現状では，多剤併用処方の有効性を支持する無作為化比較試験は限られており[9,18]，多剤併用処方に関する治療ガイドラインも整備されていない[18]．また，多剤併用処方により有害事象が増えるのも事実であり[18]，すでに，抗精神病薬と抗うつ薬の併用では体重増加[9]，抗うつ薬と抗不安・睡眠薬の併用では自殺関連事象の増加[5]，などといった有害事象が指摘されている．こうした状況下であるため，臨床家が多剤併用処方の必要性に迫られた際は，①多剤併用処方の期間を定めること，②効果と有害事象を定期的にモニタリングすること，③すべての有害事象を適切に規制当局に報告することが推奨されている[9,18]．

これまでの向精神薬の多剤併用処方のエビデンスが不足していることは明らかであり，①プラセボ対照無作為化比較試験により，多剤併用処方の有効性を検討すること[6,18]，②レセプト情報などと臨床情報を連結した臨床データベースを構築した観察研究により，実臨床のセッティングにおける多剤併用処方による長期的な有効性と安全性を検討すること[6,9,48]，が求められている．日本においても，子どもへの向精神薬の多剤併用処方の有効性と安全性の検討は不可欠であるが，それ以前に，向精神薬の多くは適応外使用であるため，まずは，治験の推進が喫緊の課題といえるであろう[13,15]．余儀なく向精神薬を適応外使用せざるを得ない状況は，医師と患者双方共に不利益をもたらすため[13]，諸外国のように小児治験を法令化することを考慮すべきであろう[17]．

3．本研究の限界

本研究は，日本全国の子どもへの向精神薬の処方状況を検討した初めての研究であるが，いくつかの限界がある．第1に，本研究における向精神薬の処方件数は，レセプトあたりの処方件数であり，向精神薬処方を受けた患者数を求められていない．すなわち，複数の診療科や医療機関を受診する人がいることを想定すると，レセプトあたりの処方件数は，患者あたりの処方件数よりも過小評価されている可能性が高い．第2に，レセプト情報では診療科情報や臨床情報の精度に限界があるため，誰が何のために向精神薬を処方したかは明らかにならない．第3に，共済組合加入者や生活保護受給者は，社会医療診療行為別調査の対象外となるため，一般化可能性に限界がある．ただし，全人口の91％は社会医療診療行為別調査の調査対象である医療保険に加入しているため[27]，本研究の知見は，おおむね日本を代表すると判断できるであろう．

Ⅳ．結　　論

子どもに対する向精神薬の適応外使用として，

抗精神病薬や抗うつ薬の処方件数が増えていること，向精神薬のクラス間多剤併用処方も高頻度でみられることが示された．適応外使用の有効性や安全性は確立していないため，治験の推進と長期的な有効性と安全性をモニタリングするための臨床データベースの構築が必要である．

なお，本論文に関連して開示すべき利益相反はない．

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Trends of Psychotropic Medication Use among Children and Adolescents in Japan : Data from the National Insurance Claims Database between 2002 and 2010

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Context : Despite evidence of an increase in the number of young patients receiving mental health treatment, most psychotropic medications have not been approved for the treatment of children and adolescents by the Ministry of Health, Labour and Welfare. There is little data available on psychotropic medication use in children and adolescents in Japan.

Objective : To establish the prevalence of psychotropic medications and multiclass psychotropic polypharmacy in outpatients aged 18 years or younger in Japan between 2002 and 2010.

Design : We used the national insurance claims database from the 2002-2010 Survey of Medical Care Activities in Public Health Insurance in Japan.

Outcome measures : Prevalence of psychotropic prescription and psychotropic polypharmacy.

Results : Our study dataset comprised 233,399 outpatient visits. Among patients aged 6-12 years between 2002-2004 and 2008-2010, there was a significant increase in the prevalence of ADHD medications (Odds Ratio [OR] 1.84 ; 95% Confidence Interval [CI] 1.33, 2.56) and antipsychotics (OR 1.58 ; 95%CI 1.06, 2.34), and a significant decrease in the prevalence of sedative-hypnotics (OR 0.67 ; 95%CI 0.46, 0.99). Among patients aged 13-18 years, there was a significant increase in the prevalence of ADHD medications (OR 2.49 ; 95%CI 1.34, 4.62), antipsychotics (OR 1.43 ; 95%CI 1.20, 1.70), and antidepressants (OR 1.37 ; 95%CI 1.09, 1.72). Medications that were most frequently involved used in combination of two or more psychotropic agents were mood stabilizer (93%), followed by antidepressants (77%), sedative-hypnotics (62%), antipsychotics (61%), and ADHD medications (17%).

Conclusion : Our study revealed an increase in the use of off-label antipsychotics and antidepressants among children and adolescents. Therefore, there is an urgent need for clinical trials to evaluate the efficacy of psychotropic medications for use in children and adolescents, and the development of a clinical database to monitor the associated long-term risks and benefits.

<Authors' abstract>

Keywords : children and adolescents, drug utilization, antipsychotics, antidepressants, ADHD

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Trends in use of psychotropic medications among patients treated with cholinesterase inhibitors in Japan from 2002 to 2010

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ABSTRACT

Background: We aimed to examine trends in the use of psychotropic medications among elderly outpatients with dementia in Japan between 2002 and 2010.

Methods: We used data from the 2002–2010 Survey of Medical Care Activities in Public Health Insurance (SMCA-PHI), a nationally representative cross-sectional survey of claims data for the month of June in every year. We included ambulatory care visits by patients aged 65 years or older who were prescribed cholinesterase inhibitors (n = 15,591), and identified use of any psychotropic medications during the survey month.

Results: In 2008–2010, the most prevalently prescribed psychotropic medications to patients with dementia were sedatives-hypnotics (37.5%), antipsychotics (24.9%), antidepressants (13.0%), and mood-stabilizers (2.9%). Between 2002–2004 and 2008–2010, use of second-generation antipsychotics (SGAs) increased from 5.0% to 12.0%, while use of first-generation antipsychotics (FGAs) decreased from 20.6% to 12.9%. These numbers resulted in a 1.1-fold increase in the adjusted prevalence of the overall use of antipsychotics. Quetiapine and risperidone use showed a 4.8- and 1.8-fold increase, respectively, while haloperidol use showed a 2.3-fold decrease.

Conclusions: Despite safety warnings against the use of antipsychotics for patients with dementia in several countries, our study revealed a slight increase in the extensive use of off-label antipsychotics over time in Japan. This finding indicates an urgent need for evaluation of the efficacy of antipsychotics for the approved treatment of severe agitation, aggression, and psychosis associated with dementia. Moreover, psychosocial interventions and antipsychotic withdrawal strategies are needed in order to reduce the overall prevalence of antipsychotic use.

Key words: dementia, behavioral and psychological symptoms of dementia (BPSD), psychopharmacology, mental health policy

Introduction

About 75% of patients with dementia experience behavioral and psychological symptoms of dementia (BPSD) such as delusions, hallucinations, agitation/aggression, depression, anxiety, apathy, and sleep disturbance (Lyketsos *et al.*, 2002). Although psychotropic medications have been extensively prescribed for the treatment of BPSD (Martinez *et al.*, 2013), there is a need for more evidence on the risks and benefits of the use of psychotropic medications.

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A number of previous studies have revealed that antipsychotics are associated with increased mortality in patients with dementia (Schneider *et al.*, 2005; Gill *et al.*, 2007). Banerjee (2009) estimated that the administration of a second-generation antipsychotic to 1,000 patients with BPSD for around 12 weeks would result in death in an additional 10 patients, cerebrovascular adverse events in an additional 18 patients, and gait disturbances in an additional 58–94 patients. Thus, some clinical practice guidelines recommend that non-pharmacological approaches should be the first line of treatment for BPSD (National Institute for Health and Clinical Excellence, 2006; Rabins *et al.*, 2007). Notwithstanding the safety issues of antipsychotics, it would be unrealistic to treat "all" patients with BPSD via a strictly non-pharmacological approach, especially when severe

aggression and agitation are present (Gareri *et al.*, 2014). A recent clinical practice guideline and a systematic review recommended aripiprazole, olanzapine, and risperidone for severe agitation, aggression, and psychosis associated with dementia when a patient is believed to be at risk of harm to self or others (Maglione *et al.*, 2011; Herrmann *et al.*, 2013). However, with the exception of carbamazepine (Yeh and Ouyang, 2012), there is insufficient evidence to recommend the use of alternative psychotropic medications for BPSD such as quetiapine (Herrmann *et al.*, 2013), antidepressants (including selective serotonin reuptake inhibitors and trazodone) (Herrmann *et al.*, 2013), benzodiazepines (BZDs) (Tampi and Tampi, 2014), and anticonvulsant mood-stabilizers (including gabapentin, lamotrigine, lithium, topiramate, and valproate) (Yeh and Ouyang, 2012; Herrmann *et al.*, 2013).

Several regulatory agencies have issued warnings and regulations regarding the prescription of antipsychotics for BPSD in patients with dementia. In 2005, the United States Food and Drug Administration (FDA) gave the strongest warning (i.e. black box warning) against the use of SGAs in patients with dementia (U.S. Food and Drug Administration, 2005). In 2008, the FDA added a similar warning for FGAs (U.S. Food and Drug Administration, 2008). Thus, there are currently no FDA-approved medications for BPSD treatment. In the United Kingdom, short-term (i.e. up to 6 weeks) treatment with risperidone is the only pharmacotherapy licensed for the treatment of persistent aggression in patients with dementia (Medicines and Healthcare Products Regulatory Agency, 2009). In addition, healthcare professionals have been asked to report all suspected risperidone related adverse effects during the treatment period. In Italy, physicians are subordinated to rules regarding the prescription of antipsychotics for patients with dementia (Agenzia Italiana del Farmaco, 2005). More specifically, patients who have been prescribed antipsychotics for BPSD are registered into a clinical database and monitored for adverse reactions every 2 months (Agenzia Italiana del Farmaco, 2005).

In Japan, there is no approved medication for BPSD treatment. However, off-label psychotropic medications are commonly prescribed for BPSD. Moreover, trends in the use of psychotropic medications might remain stable because the regulatory agency in Japan has not issued strong warnings and/or regulations regarding the prescription of psychotropic medications for BPSD. To date, there are no nationwide studies on the utilization of psychotropic medications for patients with dementia in Japan. Therefore, in the current study, we aimed to examine trends in psychotropic medications use for elderly patients with dementia in nationwide ambulatory care settings between 2002 and 2010.

Methods

Data source and setting

We used data from the Survey of Medical Care Activities in Public Health Insurance, a nationally representative cross-sectional survey of claims data, conducted annually by the Ministry of Health, Labor and Welfare (MHLW) (Statistics and Information Department, 2011). A detailed description of the SMCA-PHI has been reported elsewhere (Statistics and Information Department, 2011). The SMCA-PHI comprises of claims data for the month of June in every year. The study employed a two-stage stratified random sampling procedure with a first-selection of medical or pharmacy facilities and a second-stage sample of claims from the sampled facilities. In the present study, we obtained permission of the MHLW to use nine consecutive years of data from the SMCA-PHI between 2002 and 2010. We limited the sample to ambulatory care visits by patients aged 65 years or older who received a prescription of donepezil, which was the only approved cholinesterase inhibitor during the survey years. The only indication for the use of donepezil is Alzheimer's disease in Japan.

Since 1961, Japan has a universal healthcare system (National Institute of Population and Social Security Research, 2014). The Japan's public insurance system is composed of three types of health insurances: occupation-based, municipality-based, and a separate system for persons aged 75 years or older. All Japanese citizens are required to be enrolled in one of these insurances. A patient can pay maximum of 30% of medical and pharmacy fees, while the rest is paid thorough the public insurance. Because majority of psychotropic medications are prescription drugs rather than over-the-counter drugs, almost all patients who use psychotropic medications are reimbursed by the public insurance.

Psychotropic medications

We defined use of psychotropic medications as having at least one prescription of antipsychotics, antidepressants, mood-stabilizers, and/or sedatives-hypnotics during the survey month. We classified 101 substances into four major psychotropic classes according to one of the most popular prescription handbooks in the Japanese clinical setting

(Mizushima, 2002). A complete list of included medications is available as supplementary material (online publications only, see supplementary tables available as supplementary material attached to the electronic version of this paper at www.journals.cambridge.org/jid_IPG). Antipsychotics included both SGAs and FGAs. Antidepressants included new-generation antidepressants (NGAs) as defined in the previous study (Cipriani *et al.*, 2009), tricyclic antidepressants (TCAs), and others antidepressants. Mood-stabilizers included carbamazepine, gabapentin, lamotrigine, lithium, topiramate, and valproate similar to the previous study (Yeh and Ouyang, 2012). Sedatives-hypnotics included BZDs that were subdivided into sedative BZDs and hypnotic BZDs, z-drugs (i.e. zolpidem and zopiclone), and other sedatives-hypnotics. Etizolam was double-counted as both a sedative and hypnotic BZD because this substance has been used for both purposes.

Statistical analyses

We combined data from contiguous survey years into groups (2002–2004, 2005–2007, and 2008–2010) to derive more stable estimates. First, we estimated the proportion of visits where psychotropic medications had been prescribed by survey year group for psychotropic classes and individual psychotropic medications. Second, we conducted logistic regression analyses to examine trends in psychotropic medications. The outcome variable was whether a patient received psychotropic medications. The primary explanatory variable was survey year group. The potential confounding variables included in the models were selected based on previous literature (Carrasco-Garrido *et al.*, 2013; Ruths *et al.*, 2013) and data availability as follows: sex, age (65–74, 75–84, and 85 years or older), provider type (clinic and hospital), and pharmacy type (out-hospital and in-hospital pharmacy). We estimated odds ratios (ORs) and their 95% confidence intervals (CIs) for visits in which psychotropic medications had been prescribed (2002–2004 compared to 2005–2007, and 2002–2004 compared to 2008–2010) after simultaneously controlling for potential confounders. To increase interpretability, we changed the reference year as 2005–2008 and re-calculated ORs for psychotropic visits (2005–2008 compared to 2008–2010). Separate regressions were constructed for each level of psychotropic visit. Data were analyzed using R version 3.0.3.

Results

Between 2002 and 2010, the sample sizes of ambulatory visits ranged between 205,191 and 268,872, yielding a total of 2,191,098 visits. The prevalence of patients aged 65 years or older ranged 49.8% and 53.2%. The prevalence of donepezil use increased from 0.5% in 2002 to 2.3% in 2010 among patients age 65 years or older. There were 1.9-, 4.0-, and 6.2-fold increases in the prevalence of donepezil use among patients aged 65–74, 75–84, and 85 years or older, respectively.

The eligible study population included 15,591 patients aged 65 years or older with dementia from 2002 to 2010 (Table 1). We observed changes over time in age- and provider-composition in our study population. The proportion of patients aged 85 years or older ranged between 19.0% and 34.3%. In addition, the proportion of patients receiving treatment in a clinic ranged between 37.5% and 60.2%.

Table 2 depicts percentages and trends in outpatients with dementia with psychotropic prescriptions. Table 3 shows percentages and trends of the five psychotropic medications most prescribed broken into four major psychotropic classes.

In 2008–2010, the most prescribed psychotropic classes were sedatives-hypnotics (37.5%), antipsychotics (24.9%), antidepressants (13.0%), and mood-stabilizers (2.9%). Between 2002–2004 and 2008–2010, significant increases were evident among dementia visits with prescriptions for mood-stabilizers (OR 2.30, 95% CI 1.65–3.28), antidepressants (OR 1.30, 95% CI 1.12–1.51), antipsychotics (OR 1.14, 95% CI 1.02–1.27), and sedatives-hypnotics (OR 1.11, 95% CI 1.01–1.24).

Figure 1 shows major results of trends in antipsychotics use between 2002 and 2010. Amongst the antipsychotics, prevalent utilization of SGAs markedly increased from 5.0% to 12.0% (OR 2.95, 95% CI 2.44–3.59), while the use of FGAs declined from 20.6% to 12.9% (OR 0.71, 95% CI 0.62–0.88) between 2002–2004 and 2008–2010. In terms of individual antipsychotics, the five most prescribed antipsychotics were haloperidol, quetiapine, risperidone, sulpiride, and tiapride. The use of quetiapine dramatically increased from 1.3% in 2002–2004 to 3.8% in 2005–2007 (OR 2.95, 95% CI 2.10–4.25), and from 3.8% in 2005–2007 to 5.6% in 2008–2010 (OR 1.62, 95% CI 1.37–1.93), which resulted in a 4.8-fold increase between 2002–2004 and 2008–2010 (OR 4.78, 95% CI 3.45–6.82). In addition, the use of risperidone increased from 3.1% to 4.5% (OR 1.80, 95% CI 1.41–2.32) between 2002–2004 and 2008–2010. On the other, the use of haloperidol showed a 2.3-fold decrease from 2.9% to 1.1% (OR 0.44, 95% CI 0.32–0.60) between 2002–2004 and 2008–2010.

Amongst the antidepressants, prevalent utilization of NGAs slightly increased from 6.1% to

Table 1. Characteristics of study population

CHARACTERISTICS	TOTAL	SURVEY YEAR								
		2002	2003	2004	2005	2006	2007	2008	2009	2010
Total, *n*	15,591	691	848	1,297	1,480	1,781	2,178	2,286	2,583	2,447
Age, %										
65–74	10.6	25.3	17.2	17.3	13.8	10.6	7.6	8.2	7.4	7.1
75–84	59.5	55.7	60.3	59.3	60.2	60.4	60.2	60.1	59.5	58.6
≥ 85	29.8	19.0	22.5	23.4	26.0	29.0	32.2	31.7	33.2	34.3
Sex, %										
Male	27.8	15.8	26.4	28.1	28.9	27.5	27.1	29.5	29.2	28.5
Female	70.9	55.0	73.6	71.9	71.1	72.5	72.9	70.5	70.8	71.5
Unknown	1.3	29.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Provider, %										
Clinic	48.7	37.6	37.5	40.9	45.8	47.5	45.7	46.6	55.0	60.2
Hospital	51.3	62.4	62.5	59.1	54.2	52.5	54.3	53.4	45.0	39.8
Pharmacy, %										
Out-hospital	35.9	29.2	31.4	36.7	34.9	34.5	35.4	35.3	38.6	38.6
In-hospital	64.1	70.8	68.6	63.3	65.1	65.5	64.6	64.7	61.4	61.4

Table 2. Trends in psychotropic visits by psychotropic classes

PSYCHOTROPICS	PSYCHOTROPIC VISITS, %			ODDS RATIOS FOR TIME TREND (95% CI)		
	2002–2004	2005–2007	2008–2010	2002–2004 (vs.) 2005–2007	2005–2007 (vs.) 2008–2010	2002–2004 (vs.) 2008–2010
Antipsychotics	25.6	26.0	24.9	1.11 (0.99, 1.24)	1.03 (0.94, 1.12)	1.14 (1.02, 1.27)*
SGAs	5.0	9.1	12.0	2.02 (1.66, 2.47)*	1.46 (1.30, 1.65)*	2.95 (2.44, 3.59)*
FGAs	20.6	16.9	12.9	0.88 (0.78, 1.00)	0.80 (0.72, 0.89)*	0.71 (0.62, 0.80)*
Antidepressants	11.5	12.6	13.0	1.21 (1.04, 1.41)*	1.08 (0.96, 1.21)	1.30 (1.12, 1.51)*
NGAs	6.1	7.6	7.3	1.37 (1.13, 1.66)*	1.00 (0.87, 1.14)	1.36 (1.13, 1.65)*
TCAs	1.7	1.9	1.7	1.14 (0.80, 1.64)	1.00 (0.76, 1.32)	1.14 (0.81, 1.63)
Others	3.7	3.1	3.9	0.96 (0.74, 1.25)	1.42 (1.17, 1.74)*	1.37 (1.08, 1.75)*
Mood stabilizers	1.7	2.0	2.9	1.46 (1.02, 2.12)*	1.58 (1.24, 2.01)*	2.30 (1.65, 3.28)*
Sedatives-hypnotics	35.2	38.4	37.5	1.08 (0.97, 1.20)	1.04 (0.96, 1.12)	1.11 (1.01, 1.24)*
Any BZDs	28.5	29.6	28.6	1.02 (0.91, 1.14)	1.00 (0.92, 1.09)	1.02 (0.92, 1.14)
Sedative BZDs	13.8	14.9	13.4	1.11 (0.96, 1.28)	0.90 (0.81, 1.00)*	1.00 (0.87, 1.14)
Hypnotics BZDs	19.5	20.6	20.6	1.02 (0.90, 1.15)	1.04 (0.95, 1.14)	1.06 (0.94, 1.19)
Z-drugs	4.8	6.8	7.6	1.43 (1.17, 1.77)*	1.17 (1.01, 1.34)*	1.67 (1.37, 2.04)*
Others	1.9	2.0	1.3	1.26 (0.89, 1.82)	0.68 (0.52, 0.91)*	0.86 (0.60, 1.25)

Note. BZDs = benzodiazepines; CI = confidence interval; FGAs = first-generation antipsychotics; NGAs = new-generation antidepressants; SGAs = second-generation antipsychotics; TCAs = tricyclic antidepressants.
*$p < 0.05$.

7.3% (OR 1.36, 95% CI 1.13–1.65), and other antidepressants increased from 3.7% to 3.9% (OR 1.37, 95% CI 1.08–1.75) between 2002–2004 and 2008–2010. The five most prescribed antidepressants were fluvoxamine, mianserin, milnacipran, paroxetine, and trazodone. The use of trazodone markedly increased from 0.8% in 2002–2004 to 1.7% in 2008–2010 (OR 2.78, 95% CI 1.77–4.58). The use of paroxetine significantly increased from 2.5% in 2002–2004 to 3.5% in 2005–2007 (OR 1.51, 95% CI 1.15–2.02), and non-significantly decreased from 3.5% in 2005–2007 to 2.9% in 2008–2010, which resulted in a 1.3-fold increase between 2002–2004 and 2008–2010 (OR 1.33, 95% CI 1.01–1.77).

Amongst the mood-stabilizers, the use of lithium dramatically increased from 0.1% in 2002–2004 to 0.5% in 2008–2010 (OR 5.07, 95% CI 1.99–17.16). The use of valproate also markedly increased from 1.1% in 2002–2004 to 1.9% (OR 2.27, 95% CI 1.53–3.48).

Amongst the sedatives-hypnotics, the most prescribed subclasses were hypnotic BZDs (20.6%), Sedative BZDs (13.4%), z-drugs (7.6%), and

Table 3. Trends in psychotropic visits by individual psychotropic medications

	PSYCHOTROPIC VISITS, %			ODDS RATIOS FOR TIME TREND (95% CI)		
PSYCHOTROPICS	2002–2004	2005–2007	2008–2010	2002–2004 (vs.) 2005–2007	2005–2007 (vs.) 2008–2010	2002–2004 (vs.) 2008–2010
Antipsychotics						
Haloperidol	2.9	2.0	1.1	0.72 (0.54, 0.97)*	0.61 (0.46, 0.81)*	0.44 (0.32, 0.60)*
Quetiapine	1.3	3.8	5.6	2.95 (2.10, 4.25)*	1.62 (1.37, 1.93)*	4.78 (3.45, 6.82)*
Risperidone	3.1	3.9	4.5	1.39 (1.07, 1.80)*	1.30 (1.09, 1.56)*	1.80 (1.41, 2.32)*
Sulpiride	3.8	3.3	2.6	0.88 (0.69, 1.12)	0.80 (0.65, 0.98)*	0.70 (0.55, 0.90)*
Tiapride	9.9	9.3	7.4	0.95 (0.81, 1.11)	0.81 (0.71, 0.92)*	0.77 (0.65, 0.90)*
Antidepressants						
Fluvoxamine	2.5	2.3	1.7	1.05 (0.77, 1.44)	0.75 (0.59, 0.97)*	0.79 (0.58, 1.09)
Mianserin	1.7	1.1	1.3	0.79 (0.54, 1.18)	1.35 (0.98, 1.88)	1.07 (0.75, 1.56)
Milnacipran	1.2	1.7	1.2	1.42 (0.96, 2.14)	0.75 (0.56, 1.00)	1.06 (0.71, 1.60)
Paroxetine	2.5	3.5	2.9	1.51 (1.15, 2.02)*	0.88 (0.72, 1.07)	1.33 (1.01, 1.77)*
Trazodone	0.8	1.3	1.7	1.99 (1.24, 3.33)*	1.40 (1.05, 1.89)*	2.78 (1.77, 4.58)*
Mood stabilizers†						
Carbamazepine	0.4	0.5	0.5	1.40 (0.71, 2.96)	1.03 (0.63, 1.70)	1.44 (0.75, 3.00)
Lithium	0.1	0.3	0.5	2.34 (0.83, 8.30)	2.17 (1.19, 4.18)*	5.07 (1.99, 17.16)*
Sodium valproate	1.1	1.3	1.9	1.33 (0.87, 2.11)	1.70 (1.27, 2.29)*	2.27 (1.53, 3.48)*
Sedatives-hypnotics						
Brotizolam	4.7	4.4	5.6	0.91 (0.73, 1.14)	1.34 (1.14, 1.58)*	1.22 (0.99, 1.50)
Etizolam	4.9	6.0	5.4	1.23 (1.00, 1.53)*	0.91 (0.79, 1.06)	1.13 (0.92, 1.39)
Triazolam	2.3	2.9	2.8	1.19 (0.89, 1.61)	0.94 (0.76, 1.16)	1.12 (0.85, 1.51)
Zolpidem	2.0	3.3	4.5	1.54 (1.15, 2.11)*	1.36 (1.13, 1.64)*	2.10 (1.59, 2.83)*
Zopiclone	2.8	3.5	3.1	1.36 (1.04, 1.80)*	0.97 (0.80, 1.19)	1.33 (1.02, 1.75)*

Note. BZDs = benzodiazepines; CI = confidence interval; FGAs = first-generation antipsychotics; NGAs = new-generation antidepressants; SGAs = second-generation antipsychotics; TCAs = tricyclic antidepressants.
*$p < 0.05$.
†Gabapentin and topiramate were prescribed for only one patient, respectively. Lamotrigine was not prescribed.

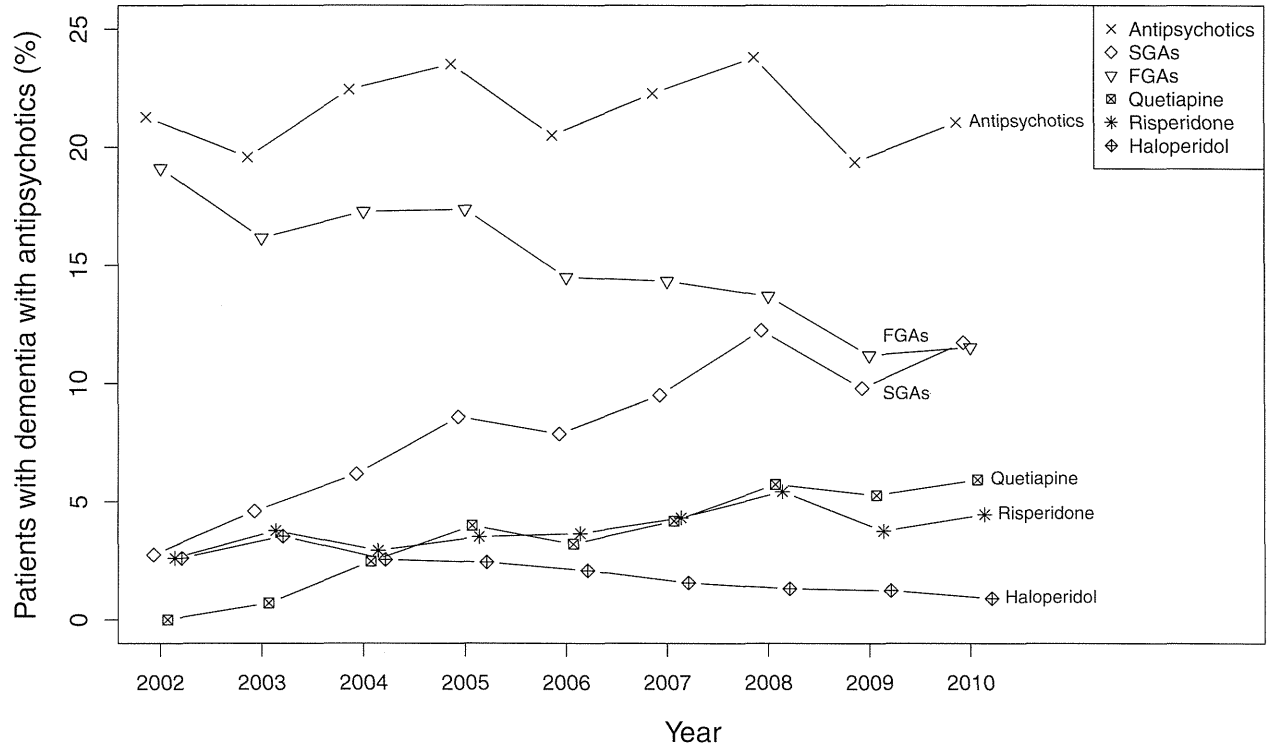

Figure 1. Trends in antipsychotics use between 2002 and 2010.

other sedatives-hypnotics (1.3%) in 2008–2010. Between 2002–2004 and 2008–2010, the prevalent utilization of z-drugs increased from 4.8% to 7.6% (OR 1.67, 95% CI 1.37–2.04) although use of any BZDs, sedative BZDs, hypnotic BZDs, and other sedatives-hypnotics remained stable. The use of zolpidem and zopiclone increased, respectively, from 2.0% to 4.5% (OR 2.10, 95% CI 1.59–2.83), and from 2.8% to 3.1% (OR 1.33, 95% CI 1.02–1.75) between 2002–2004 and 2008–2010.

Discussion

Our study yielded six major findings using data collected from outpatients with dementia. First, we observed a 1.1-fold increase in the extensive use of antipsychotics (about 25%) over time. Our findings are inconsistent with those of several previous studies that found decreasing trends in overall antipsychotic use in patients with dementia, although direct comparison is difficult because of differences in study designs and outcomes. These prior studies reported a 69% reduction from 1995 to 2011 in the United Kingdom (Martinez *et al.*, 2013), a 41% reduction from 1999 to 2007 in the United States of America (Kales *et al.*, 2011), a 40% reduction from 2003 to 2011 in France (Gallini *et al.*, 2014), a 34% reduction from 2002 to 2008 in Italy (Franchi *et al.*, 2012), and a non-significant 9% reduction from 2004 to 2009 in Germany (Schulze *et al.*, 2013). This discrepancy may be because the regulatory agency in Japan has not yet issued strong warnings and regulations regarding the prescription of psychotropic medications for BPSD. Our results might prompt the regulatory agency to issue safety warnings. The contents of such warnings would be optimal only if they provide physicians with guidelines and alternative treatment strategies for the management of BPSD (Gallini *et al.*, 2014). However, some nursing home facilities have reported their inability to provide alternative treatment strategies for residents with BPSD (Nakanishi *et al.*, 2012). To reduce the overall use of antipsychotics, systematic efforts should be made to ensure that physicians and nursing staff can incorporate evidence-based approaches such as antipsychotic withdrawal strategies (Declercq *et al.*, 2013) and psychosocial interventions (Richter *et al.*, 2012) into their routine clinical practices.

Second, there was a significant shift in the prevalence of prescriptions from FGAs to SGAs. Among the various types of antipsychotics, use of quetiapine and risperidone increased, while that of haloperidol decreased. This shift is likely desirable because FGAs have been associated with a greater mortality rate than SGAs (Gill *et al.*, 2007). However, based on the available evidence, the strength of recommendations varies amongst individual SGAs. A recent clinical practice guideline and systematic review suggested that there is insufficient evidence for or against the use of quetiapine (Herrmann *et al.*, 2013); on the other hand, several previous studies have provided sufficient evidence to recommend the use of aripiprazole, olanzapine, and risperidone (Maglione *et al.*, 2011; Herrmann *et al.*, 2013). In Japan, these SGAs are approved only for the treatment of patients with schizophrenia and bipolar disorders. In addition, no randomized placebo-controlled trials have been conducted to examine the efficacy of antipsychotics for BPSD in Japan. These results suggest the urgent need to evaluate the efficacy of antipsychotics for the approved treatment of severe BPSD.

Third, we observed a stable non-negligible use of sedative BZDs (13%) over time. A systematic review showed that there is inadequate data for recommending the routine use of sedative BZDs for BPSD (Tampi and Tampi, 2014). A clinical practice guideline indicated that the side effects associated with sedative BZDs outweighed the benefits when compared to antipsychotic medications (Rabins *et al.*, 2007). The common side effects of BZDs include over-sedation, ataxia, amnesia, confusion (even delirium), and possibly paradoxical anxiety, which lead to worsening cognition and behavior and increasing risk of falls (Rabins *et al.*, 2007). In addition, the guideline stated that sedative BZDs could be useful on an occasional (as-needed) basis for patients who only have rare episodes of agitation or for those needing to be sedated for a particular procedure such as a tooth extraction (Rabins *et al.*, 2007). This suggests that physicians should be judicious in their prescription of sedative BZDs for BPSD. Direct-to-consumer education about the risks of BZDs use and a stepwise tapering protocol might be a promising strategy to discontinue the use of BZDs (Tannenbaum *et al.*, 2014).

Fourth, we found significant increases in the use of lithium and valproate over time. The prevalent utilization of lithium is relatively low (0.5%), while the prevalent utilization of valproate is non-negligible (1.9%). Especially, the latter prescribing practice might be incongruent with recommendations from the current available evidence. More specifically, strong evidence indicates that valproate should not be used for BPSD due to its lack of efficacy and risk of mortality (Yeh and Ouyang, 2012; Herrmann *et al.*, 2013). Thus, our results should raise caution to frequent prescribers of valproate for patients with BPSD.

Fifth, we observed an increase in the use of antidepressants over time, especially trazodone and paroxetine. It is difficult to judge whether these prescription patterns are clinically questionable due to the lack of available data in the literature. It has been suggested that there is sufficient evidence to recommend the use of these antidepressants to manage major depressive disorders; however, there is insufficient evidence for or against the use of trazodone or selective serotonin reuptake inhibitors in the management of agitated patients (Herrmann *et al.*, 2013). A meta-analysis of seven randomized controlled trials concluded that few high-quality studies have examined the efficacy and acceptability of antidepressants for BPSD treatment, although antidepressants may have the potential to improve symptoms of agitations and psychosis in patients with dementia (Seitz *et al.*, 2011). Therefore, large randomized controlled trials are needed to determine the efficacy and acceptability of antidepressants for BPSD management.

Sixth, the use of z-drugs showed a 1.7-fold increase over time, while the use of hypnotic BZDs remained stable. The possible reason for the increasing trend in z-drug use is that physicians might perceive z-drugs as being more effective and safer compared to BZDs (Hoffmann, 2013); however, there is no evidence to support this assumption (Levy, 2014). Moreover, a recent systematic review showed that there is very little data regarding appropriate medication selection for sleep disturbances in patients with dementia (McCleery *et al.*, 2014). These results indicate an urgent need for evaluating the efficacy and safety of medications commonly used for sleep disturbances in patients with dementia.

Limitations

Our study had four important limitations. First, the data available to us did not include information on diagnosis, duration of treatments, dosage, or adherence. As a result, we were unable to determine the reasons why physicians prescribed psychotropic medications. More specifically, we were unable to exclude patients who had severe and enduring mental illness such as schizophrenia or severe bipolar disorders and were likely to receive psychotropic medications for indications other than BPSD. Second, our study population did not represent the whole population of patients with dementia, because our criterion for identifying patients with dementia was limited to a prescription of cholinesterase inhibitors. Third, we were unable to investigate the possibility of change in the eligible study population over time, although we adjusted for potential cofounding variables such as sex, age, provider type, and pharmacy type. For example, we observed a marked increase in the use of donepezil over time. One possible explanation for the increase is that physicians become more familiar with the use of donepezil that have been approved for the treatment of Alzheimer's disease since 1998. Another possible explanation is due to the increase in off-label use of donepezil for the treatment of other conditions such as vascular dementia and dementia with Lewy bodies. Fourth, the use of psychotropic medications may have been underestimated due to the nature of the data; we were unable to identify patients who received cholinesterase inhibitors and psychotropic medications from different pharmacies or from different departments within the same medical facility.

Conclusions

In conclusion, we found a slight increase in the extensive use of off-label antipsychotics over time. This study highlights the urgent need to evaluate the efficacy of antipsychotics for the approved treatment of severe BPSD. Moreover, our findings suggest the need to direct cares and resources toward psychosocial interventions and antipsychotic withdrawal strategies in order to reduce the overall prevalence of the use of antipsychotics.

Conflict of interest

None.

Description of authors' roles

Y. Okumura participated in the study concept and design, analysis and interpretation of data, and drafting of the manuscript. T. Togo and J. Fujita participated in supervision of the study design, interpretation of data, and critical revision of the manuscript for important intellectual content. All authors contributed to and approved the final manuscript.

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Supplementary material

To view supplementary material for this article, please visit http://dx.doi.org/10.1017/S1041610214001975

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Supplementary Table. Complete list of psychotropic medications

Generic name	Survey year
SGAs	
aripiprazole	2007-2010
blonanserin	2008-2010
clozapine	2010-2010
olanzapine	2002-2010
perospirone	2002-2010
quetiapine	2002-2010
risperidone	2002-2010
FGAs	
bromperidol	2002-2010
carpipramine	2002-2010
chlorpromazine	2002-2010
chlorpromazine-promethazine-combined	2002-2010
clocapramine	2002-2010
fluphenazine	2002-2010
haloperidol	2002-2010
haloperidol decanoate	2002-2010
levomepromazine	2002-2010
moperone	2002-2009
mosapramine	2002-2010
nemonapride	2002-2010
oxypertine	2002-2010
perphenazine	2002-2010
pimozide	2002-2010
pipamperone	2002-2010
prochlorperazine	2002-2010
propericiazine	2002-2010
spiperone	2002-2010
sulpiride	2002-2010
sultopride	2002-2010
thioridazine	2002-2006
tiapride	2002-2010
timiperone	2002-2010
trifluoperazine	2002-2010
zotepine	2002-2010
NGAs	
duloxetine	2010-2010
milnacipran	2002-2010
mirtazapine	2010-2010
paroxetine	2002-2010
sertraline	2007-2010
fluvoxamine	2002-2010
TCAs	
amitriptyline	2002-2010
amoxapine	2002-2010
clomipramine	2002-2010
dosulepin	2002-2010
imipramine	2002-2010
lofepramine	2002-2010
nortriptyline	2002-2010
trimipramine	2002-2010
Other antidepressants	
maprotiline	2002-2010
mianserin	2002-2010
setiptiline	2002-2010
trazodone	2002-2010
Mood-stabilizers	
carbamazepine	2002-2010
gabapentin	2007-2010
lamotrigine	2009-2010

Supplementary Table. Complete list of psychotropic medications

Generic name	Survey year
lithium	2002-2010
topiramate	2008-2010
valproate	2002-2010
Sedative BZDs	
alprazolam	2002-2010
bromazepam	2002-2010
chlordiazepoxide	2002-2010
clorazepate dipotassium	2002-2010
clotiazepam	2002-2010
cloxazolam	2002-2010
diazepam	2002-2010
ethyl loflazepate	2002-2010
etizolam*	2002-2010
fludiazepam	2002-2010
flutazolam	2002-2010
flutoprazepam	2002-2010
lorazepam	2002-2010
medazepam	2002-2010
mexazolam	2002-2010
oxazolam	2002-2010
prazepam	2002-2010
tofisopam	2002-2010
Hypnotic BZDs	
brotizolam	2002-2010
estazolam	2002-2010
etizolam*	2002-2010
flunitrazepam	2002-2010
flurazepam	2002-2010
haloxazolam	2002-2010
lormetazepam	2002-2010
nimetazepam	2002-2010
nitrazepam	2002-2010
quazepam	2002-2010
rilmazafone	2002-2010
triazolam	2002-2010
Z-drugs	
zolpidem	2002-2010
zopiclone	2002-2010
Other sedatives-hypnotics	
amobarbital	2002-2010
barbital	2002-2010
bromovalerylurea	2002-2010
calcium bromide	2002-2010
chloral	2002-2010
hydroxyzine	2002-2010
passiflamin	2002-2008
pentobarbital calcium	2002-2010
phenobarbital	2002-2010
phenobarbital sodium	2002-2010
secobarbital sodium	2002-2010
tandospirone citrate	2002-2010
triclofos	2002-2010

Note. BZDs = benzodiazepines; CI = confidence interval; FGAs = first-generation antipsychotics; NGAs = new-generation antidepressants; SGAs = second-generation antipsychotics; TCAs = tricyclic antidepressants.
* Etizolam was double-counted as both a sedative and hypnotic BZD.

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CORRIGENDUM

Trends in use of psychotropic medications among patients treated with cholinesterase inhibitors in Japan from 2002 to 2010 — Corrigendum

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In the above published article by Okumura *et al.*, the authors apologize for errors in the 2nd, 3rd and 4th columns of Table 2. The corrected Table 2 is given below.

Table 2 Trends in psychotropic visits by psychotropic classes

	PSYCHOTROPIC VISITS,%			ODDS RATIOS FOR TIME TREND (95% CI)		
PSYCHOTROPICS	2002–2004	2005–2007	2008–2010	2002–2004 VERSUS 2005–2007	2005–2007 VERSUS 2008–2010	2002–2004 VERSUS 2008–2010
Antipsychotics	21.3	22.0	21.3	1.11 (0.99, 1.24)	1.03 (0.94, 1.12)	1.14 (1.02, 1.27)*
SGAs	4.9	8.7	11.2	2.02 (1.66, 2.47)*	1.46 (1.30, 1.65)*	2.95 (2.44, 3.59)*
FGAs	17.4	15.2	12.1	0.88 (0.78, 1.00)	0.80 (0.72, 0.89)*	0.71 (0.62, 0.80)*
Antidepressants	10.4	11.3	11.4	1.21 (1.04, 1.41)*	1.08 (0.96, 1.21)	1.30 (1.12, 1.51)*
NGAs	6.0	7.5	7.1	1.37 (1.13, 1.66)*	1.00 (0.87, 1.14)	1.36 (1.13, 1.65)*
TCAs	1.7	1.7	1.7	1.14 (0.80, 1.64)	1.00 (0.76, 1.32)	1.14 (0.81, 1.63)
Others	3.6	3.0	3.8	0.96 (0.74, 1.25)	1.42 (1.17, 1.74)*	1.37 (1.08, 1.75)*
Mood stabilizers	1.6	1.9	2.8	1.46 (1.02, 2.12)*	1.58 (1.24, 2.01)*	2.30 (1.65, 3.28)*
Sedatives-hypnotics	25.7	27.1	27.3	1.08 (0.97, 1.20)	1.04 (0.96, 1.12)	1.11 (1.01, 1.24)*
Any BZDs	21.7	22.1	21.8	1.02 (0.91, 1.14)	1.00 (0.92, 1.09)	1.02 (0.92, 1.14)
Sedative BZDs	12.1	13.2	11.9	1.11 (0.96, 1.28)	0.90 (0.81, 1.00)*	1.00 (0.87, 1.14)
Hypnotics BZDs	16.7	17.0	17.2	1.02 (0.90, 1.15)	1.04 (0.95, 1.14)	1.06 (0.94, 1.19)
Z-drugs	4.7	6.6	7.4	1.43 (1.17, 1.77)*	1.17 (1.01, 1.34)*	1.67 (1.37, 2.04)*
Others	1.7	1.9	1.3	1.26 (0.89, 1.82)	0.68 (0.52, 0.91)*	0.86 (0.60, 1.25)

Note. BZDs = benzodiazepines; CI = confidence interval; FGAs = first-generation antipsychotics; NGAs = new-generation antidepressants; SGAs = second-generation antipsychotics; TCAs = tricyclic antidepressants.
* $p < .05$

The following corrections related to Table 2 have also been made to the article:

ABSTRACT (Results)

Results: In 2008–2010, the most prevalently prescribed psychotropic medications to patients with dementia were sedatives-hypnotics (27.3%), antipsychotics (21.3%), antidepressants (11.4%), and mood-stabilizers (2.8%). Between 2002–2004 and 2008–2010, use of second-generation antipsychotics increased from 4.9% to 11.2%, while use of first-generation antipsychotics decreased from 17.4% to 12.1%.

Results: (paragraph 4)

In 2008–2010, the most prescribed psychotropic classes were sedatives-hypnotics (27.3%), antipsychotics (21.3%), antidepressants (11.4%), and mood-stabilizers (2.8%).

Results: (paragraph 5)

Figure 1 shows major results of trends in antipsychotics use between 2002 and 2010. Amongst the antipsychotics, prevalent utilization of SGAs markedly increased from 4.9% to 11.2% (OR 2.95, 95% CI 2.44–3.59), while the use of FGAs declined from 17.4% to 12.1% (OR 0.71, 95% CI 0.62–0.80) between 2002–2004 and 2008–2010.

Results: (paragraph 6)

Amongst the antidepressants, prevalent utilization of NGAs slightly increased from 6.0% to 7.1% (OR 1.36, 95% CI 1.13–1.65), and other antidepressants increased from 3.6% to 3.8% (OR 1.37, 95% CI 1.08–1.75) between 2002–2004 and 2008–2010.

Results: (paragraph 8)

Amongst the sedatives-hypnotics, the most prescribed subclasses were hypnotic BZDs (17.2%), Sedative BZDs (11.9%), z-drugs (7.4%), and other sedatives-hypnotics (1.3%) in 2008–2010. Between 2002–2004 and 2008–2010, the prevalent utilization of z-drugs increased from 4.7% to 7.4% (OR 1.67, 95% CI 1.37–2.04) although use of any BZDs, sedative BZDs, hypnotic BZDs, and other sedatives-hypnotics remained stable.

Discussion (paragraph 1)

Our study yielded six major findings using data collected from outpatients with dementia. First, we observed a 1.1-fold increase in the extensive use of antipsychotics (about 21%) over time.

Discussion (paragraph 3)

We observed a stable non-negligible use of sedative BZDs (12%) over time.

The corrections do not alter the conclusions of this article and the authors regret these errors.

Reference

Okumura, Y., Togo, T. and Fujita, J. Trends in use of psychotropic medications among patients treated with cholinesterase inhibitors in Japan from 2002 to 2010. *International Psychogeriatrics*, Published online, 12 September 2014, doi: 10.1017/S1041610214001975.