

## Prescribing Trends Psychotropic Drugs Against Children and Adolescents and Association with Polypharmacy Reduction Policy for Psychotropic Drugs: Based on Japanese National Database Survey

Jinsang Park<sup>a</sup>, Tasuku Okui<sup>b</sup>, Naoki Nakashima<sup>b</sup>

<sup>a</sup> Department of Pharmaceutical Sciences, International University of Health and Welfare, Fukuoka Japan

<sup>b</sup> Kyushu University Hospital, Medical Information Center, Fukuoka Japan

### Abstract

*In Japan, the polypharmacy reduction policy for psychotropic drugs is intended to reduce the reimbursement of medical costs when “three or more types of psychotropic drugs” are prescribed. However, non-polypharmacy patients who need multiple drugs are also comprehensively evaluated. This study demonstrated that the polypharmacy reduction policy for psychotropic drugs is associated with reductions of the amounts of in-hospital prescriptions for patients using antidepressants, antipsychotics, anxiolytics, and benzodiazepines.*

### Keywords:

Polypharmacy, National Database, Psychopharmacology

### Introduction

Childhood and adolescence are crucial time of biological, psychological, and social environmental factors for biopsychosocial development. Over the last two decades, the clinical trial data support the interventions based on early psychotherapeutic and psychosocial interventions. Thus, the use of psychotropic drugs necessary to treat severe mental disorders in children and adolescents has dramatically increased and, more recently, these clinical trial data have been subjected to analytic evaluations [1]. However, despite the evidence of the efficacy of several psychotropic drugs, the duration of untreated illness in mental disorders is long, which adversely affects the long-term outcomes that result in subjective distress, which dramatically increased in youth. Moreover, psychotropic polypharmacy is also common in pediatric clinical practice and increases the risk of adverse events and drug-drug interactions. In fact, benzodiazepine receptor agonists (BZs) have a high potential for tolerance, dependence, and misuse, as well as adverse events, including cognitive impairment, accidents, and falls [2]. The Ministry of Health, Labor, and Welfare Japan reported 270,000 as of the total number of patients with mental disorders under the age of 20 in Japan in 2017, which is about two times higher compared to the number in 2002. The number of children prescribed with psychotropic drugs is expected to increase in Japan. Moreover, it is expected that they will be prescribed psychotropic drugs with efficacy and safety already not yet been completely established for the administration in children and adolescents. In Japan, the polypharmacy reduction policy for psychotropic drugs introduced is intended to reduce the reimbursement of medical costs when “three or more types of psychotropic drugs” are prescribed. The policy for multidrug prescriptions started in 2000, and the policy for multidrug psychotropic drugs was introduced around 2014. However, non-polypharmacy patients who need multiple drugs are also com-

prehensively evaluated within the same criteria of a drug insurance claim. This study aims to examine the impact of the polypharmacy reduction policy on the amounts of psychotropic drug prescriptions in children, using a large-scale Japanese national healthcare claims database.

### Methods

This study conducted a trend analysis for the amounts of psychotropic drug prescriptions in children and adolescent (0–19 years old) outpatients. The open data were obtained from the National Database (NDB) of Health Insurance Claims and Specific Health Checkups of Japan between April 2015 and March 2019. NDB is governed by the Ministry of Health and Welfare and Labour in Japan, and it collects health insurance claims data from almost all patients who received medical care services under the national health insurance system in Japan (Figure 1). This system covers more than 126 million people and 1.9 billion claims annually [3]. The data were aggregated by the type of psychotropic drugs, namely antidepressants, antipsychotics, anxiolytics, hypnotics, and BZs. The prescribed amount of each type of psychotropic drug was calculated by age group, year, sex, and in- or out-of-hospital prescription, taking into account of dose equivalences of different drugs. The standard drug-equivalent amounts (mg) for each type of psychotropic drug were calculated by setting a standard drug. In addition, whether the prescribed amount increased or decreased over the years was also evaluated for each type of psychotropic drug by a linear regression model. Age and sex were adjusted in the analysis, being all the analyses conducted by in- or out-of-hospital prescription. All statistical tests were two-sided, and *p*-values of <0.05 were considered statistically significant. All the analyses were performed using R software (version 3.6.3).

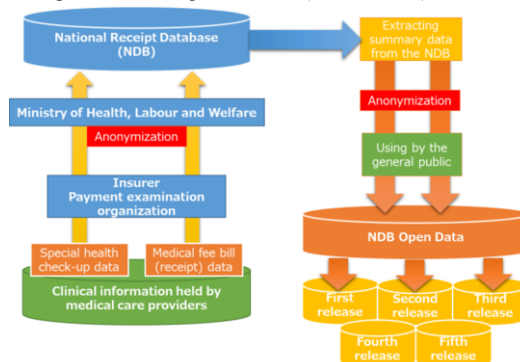


Figure 1. Overview of NDB open data aggregation

## Results

The data of 26 types of BZs, 16 types of antidepressants, 11 types of antipsychotics, 18 types of anxiolytics, and 16 types of hypnotics were available. As shown in Table 1, the prescription trends differed depending on the types of psychotropic drugs and in or out-of-hospital prescriptions. As demonstrated in Table 2, the prescribed amounts tended to decrease over the years for in-hospital prescriptions, including hypnotics ( $P$ -value = 0.002), whereas the opposite tendency was observed for out-of-hospital prescriptions for psychotropic drugs. Linear regression analysis showed that the out-of-hospital prescribed amounts of antidepressants and hypnotics tended to increase over the years. On the other hand, a decreasing trend was observed in the prescribed amounts of different prescriptions, including BZs, antipsychotics, and anxiolytics, in the out-of-hospital setting.

Table 1. The prescribed amount of each type of psychotropic drug against ages of 0–19 from 2015 to 2018

	In-hospital		Out-of-hospital	
	Male	Female	Male	Female
<b>Sertraline-equivalent doses for Antidepressants (mg)</b>				
<b>2015</b>	23,344,658	24,733,283	165,440,179	193,902,850
<b>2016</b>	20,901,277	21,809,922	158,280,217	182,759,836
<b>2017</b>	21,111,263	24,570,730	170,103,081	205,302,180
<b>2018</b>	19,586,052	24,253,917	174,582,104	221,682,661
<b>Chlorpromazine-equivalent doses for Antipsychotics (mg)</b>				
<b>2015</b>	174,602,486	108,875,790	1,118,381,379	678,334,665
<b>2016</b>	179,060,080	100,154,244	1,077,596,521	608,485,181
<b>2017</b>	169,384,075	88,404,476	734,521,309	389,171,521
<b>2018</b>	150,697,744	73,187,797	1,034,645,452	526,317,912
<b>Diazepam-equivalent doses for Anxiolytics (mg)</b>				
<b>2015</b>	2,509,363	3,538,504	11,711,273	17,600,828
<b>2016</b>	2,266,628	3,122,410	11,381,742	16,997,723
<b>2017</b>	1,928,954	2,958,133	11,527,577	17,073,738
<b>2018</b>	1,936,643	2,883,840	11,242,484	17,013,684
<b>Haloxazolam-equivalent doses for Hypnotics (mg)</b>				
<b>2015</b>	15,938,731	13,448,692	33,943,490	33,417,570
<b>2016</b>	15,329,401	12,276,897	77,054,970	65,862,350
<b>2017</b>	14,779,136	11,405,853	8,902,531	12,321,271
<b>2018</b>	13,886,460	10,558,035	59,448,037	52,818,420
<b>Diazepam-equivalent doses for BZs (mg)</b>				
<b>2015</b>	3,148,105	4,744,634	16,880,453	26,464,407
<b>2016</b>	2,742,586	4,123,260	16,374,496	25,556,855
<b>2017</b>	2,593,870	4,050,860	15,428,163	25,044,541
<b>2018</b>	2,396,915	3,851,946	15,376,772	25,238,286

Abbreviation legend: BZs= Benzodiazepines

Table 2. Results of regression analysis evaluating the effect of years on prescribed amounts

Drugs	In-hospital	Out-of-hospital
	Slope ( $p$ -values)	Slope ( $p$ -values)
<b>Antidepressants</b>	-0.019 (0.604)	0.034 (0.364)
<b>Antipsychotics</b>	-0.077 (0.114)	-0.085 (0.170)
<b>Anxiolytics</b>	-0.064 (0.146)	-0.008 (0.860)
<b>Hypnotics</b>	0.147 (0.002)	0.025 (0.878)
<b>BZs</b>	-0.053 (0.260)	-0.017 (0.733)

Abbreviation legend: BZs= Benzodiazepines,  $p$ -value < 0.05

## Conclusions

The present study identified the trends in which prescriptions claims have changed based on drug insurance claim criteria, elucidating the relationship between the polypharmacy reduction policy interventions in the psychotropic drugs field. The present study suggests that psychotropic polypharmacy might be more associated with an increased amount of out-of-hospital prescriptions than in-hospital based on the adjusted proportions obtained using the linear regression techniques. In Japan, many acute medical institutions also provide in-hospital prescriptions. Therefore, it is suggested that the reduction effect is due to the drug reduction efforts of acute medical institutions, which have a large number of patients with high severity. Taken together, the findings of this study reinforce the importance of addressing unnecessary high-dose prescription treatment, as well as patients receiving above the clinically recommended doses. In summary, health and regulation professionals need to take further actions to effective interventions associated with reducing the number of psychotropic drugs based on clinical guidelines should also be considered in children and adolescents.

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## Address for correspondence

Jinsang Park, Ph.D. 137-1 Enokizu, 831-8501, Okawa, Fukuoka, Japan. Department of Pharmaceutical Sciences, International University of Health and Welfare.  
Email: park21@iuhw.ac.jp