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Original Article

The Prevalence and Characteristics of Older Japanese Adults with Polypharmacy, Based on Regionally Representative Health Insurance Claims Data

Hoichi Amano[a,b], Kenichi Fujimoto[a], Makoto Fujimori[a], Natsumi Saka[c], Kyoko Nomura[a,d], and Shinichi Tanihara[a,e*]

[a]*Graduate School of Public Health, Teikyo University, Itabashi-ku, Tokyo 173-8605, Japan,*
[b]*Department of Social and Behavioral Sciences, Harvard. T.H. Chan School of Public Health, Boston, MA 02115, USA,*
[c]*Department of Orthopaedic Surgery, Teikyo University School of Medicine, Itabashi-ku, Tokyo 173-8605, Japan,*
[d]*Department of Environmental Health Science and Public Health, Akita University Graduate School of Medicine, Akita-city, Akita 010-8543, Japan,* [e]*Department of Public Health, School of Medicine, Kurume University, Kurume-city, Fukuoka 830-0011, Japan*

We aimed to clarify the prevalence of polypharmacy among elderly individuals in Japan. We used the data obtained from a large-scale population-based representative database of health insurance claims in a single prefecture in Japan. We examined all of the outpatient and pharmaceutical health insurance claims for National Health Insurance and those for Late-stage Elderly Health Insurance in Nagasaki Prefecture, Japan between April and June 2016. When two or more claim forms were issued for a patient in a single month, we combined the data and identified the number of prescribed drugs for each person. The definition of polypharmacy is a the prescription of six or more drugs per month. We investigated the prevalence of polypharmacy among the beneficiaries of the two insurance systems. Of the 605,406 beneficiaries of the 2 insurance systems, 121,033 (20.0%) patients with polypharmacy were identified. The prevalence of polypharmacy increased with age, especially among the beneficiaries aged >85 years, with about half of the beneficiaries having polypharmacy status. About half of the people aged >85 years in the database had polypharmacy status. When a drug is prescribed to an elderly individual, it is necessary to consider the possibility of polypharmacy-related problems.

Key words: health insurance claims, late-stage elderly health insurance, national health insurance, Japan, polypharmacy

A reduction of unnecessary healthcare such as the overutilization of services, the overuse of medications, and overtreatment is a global challenge. The overuse of medicine may result not only in disease or disorders but also in a higher volume of healthcare provided, at a higher cost than is appropriate [1,2]. A reduction in overused tests and treatments is thus recommended [3].

Japan is a 'super-aging' society, as is rapidly becoming the case in many nations, and information gained about unnecessary healthcare in Japan will be useful worldwide. Polypharmacy, a type of unnecessary healthcare that is considered a risk factor for complications among elderly people [4-6], is defined as taking 6 or more drugs [7]. The number of elderly people (especially those aged ≥75 years) who have many chronic diseases has increased and consequently, so has the

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*Corresponding author. Phone: +81-942-31-7553; Fax: +81-942-31-4389
E-mail: tanihara_s@med.kurume-u.ac.jp (S. Tanihara)

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chance of these adults receiving fragmented and overlapping medical services from multiple medical institutions [8].

Based on an analysis of the data of hospitalized patients at acute care hospitals in Japan (2,412 records, mean age: 78.1 years), older patients taking 6 or more drugs had a higher risk of adverse drug reactions [9]. Another study showed that geriatric outpatients taking five or more drugs were at a high risk of falls [10]. Only a few reports have described a population-representative prevalence or the number of patients with polypharmacy in Japan, and these studies had small sample sizes and were limited to patients in specific medical institutions [9, 10].

Japan has provided universal healthcare coverage for over half a century, across several types of health insurance systems [11]. Under the Japanese system, health insurance claim (HIC) data have recently been used for the identification of healthcare profiles, including patient counts and treatment status, in large populations [12]. The health insurance system in Japan is broadly classified into three public systems: the National Health Insurance (NHI), Employees' Health Insurance (EHI), and Late-stage Elderly Health Insurance (LEHI) [11]. The NHI is generally operated at the municipal level and covers self-employed workers as well as unemployed and retired individuals. The EHI covers salaried workers in companies and factories and their dependents. The NHI and EHI cover all eligible individuals aged <75 years, and the LEHI covers all individuals aged ≥ 75 years, regardless of their employment status.

For the LEHI, the administrative entity is the union of the late-stage elderly residents' medical care system established in each of Japan's 47 prefectures, to which all municipalities join. Medical facilities issue claims for the reimbursement of costs of healthcare services in a given calendar month, excluding monthly copayments, according to the patients' health insurance package. The NHI organizations, which are located in the same prefecture as the medical facilities, investigate HICs to determine (1) the patient's qualification status and (2) if the healthcare services provided meet the regulations of the reimbursement rules [13].

We were thus able to conduct analyses if the entire population of elderly people living in a specific region by using the HICs in the NHI and LEHI systems. The data that we analyzed covered an entire prefecture whose population is over 1 million (Nagasaki Prefecture). Our present analyses differed from those of previous studies, which were limited to data from specific medical institutions [9, 10].

Although there have been investigations of health insurance claims data, most of the investigations used data from the NHI [14], EHI [15], or the Diagnosis Procedure Combination data [16] for analysis. There have been few studies using LEHI data. We conducted the present study to determine the prevalence of polypharmacy among elderly people in a Japanese prefecture by using a large-scale population-based HIC database's data.

Materials and Methods

Study design and data source. This study was conducted in Nagasaki Prefecture, and the study population comprised all of the beneficiaries of the NHI and LEHI in Nagasaki Prefecture. The prefecture is the southernmost of the 4 main islands of Japan, where 1.34 million people resided in a 4,093-km^2 region. As of April 2016, the prefecture had a total number of 1,395,120 residents, and the numbers of NHI and LEHI beneficiaries were 393,137 and 212,269, respectively.

This was a population-based retrospective descriptive study using HIC information. We included all of the NHI and LEHI outpatient and pharmaceutical HIC data for the prefecture from April to June 2016. Under a research agreement with the Federation of Health Insurance Organizations in Nagasaki Prefecture, information that could identify individuals such as names, the identification number of the insured person, and dates of birth was anonymized, and we created new identification codes to sum up the information of the HICs by using the hash function.

When individual beneficiaries moved from the NHI to the LEHI, the Federation of Health Insurance Organizations in Nagasaki Prefecture connected the information of the individual's qualification status for both the NHI and LEHI in order to create the new identification codes. We were thus able to establish a system that did not contain any information that could identify the personal information of the beneficiaries. The data obtained included the patients' age and sex, information on the number of drugs prescribed, and information on the pharmacy fee and pharmaceutical fee scores. We identified persons who received drug prescriptions among all insured person, and we nar-

rowed down the analysis to persons with polypharmacy, *i.e.*, using 6 or more drugs in a single month.

This study was carried out in accordance with the Declaration of Helsinki and was approved by the ethics committee of Teikyo University (approval no. 17-032) and Kurume University (approval no. 18140).

Definition of polypharmacy. In Japan, prescriptions are commonly obtained at a hospital or clinic, and medicines are then dispensed at pharmacies outside the medical facilities. These are referred to as out-of-hospital prescriptions. In some cases, medicines are obtained at pharmacies inside a hospital or clinic. These are referred to as in-hospital prescriptions.

From April to June 2016, by using the HIC data of both in- and out-of-hospital prescriptions, we summed all of the prescribed drugs including both internal and external medicines issued to each insured person for each calendar month. We then summed the number of prescribed medicines from April to June to calculate the average number of prescribed drugs for each insured person. During the study period, polypharmacy was defined as taking 6 or more drugs per month, based on a previous study and the guidelines of the Japan Geriatrics Society [7, 8].

Based on the average number of drugs prescribed, an average monthly number of six or more drugs was regarded as polypharmacy status. The average monthly number of drugs is presented for the following reasons: (1) A study on long-term (>2 months) drug prescriptions is also being conducted in Japan; (2) we combined the outside and in-hospital prescriptions; and (3) even if duplicate drugs were prescribed by different medical facilities, each drug could be counted.

Persons with prescriptions and insured persons. 'Persons with prescriptions' were defined as those prescribed one or more drugs during the follow-up period. 'Insured persons' were defined as NHI or LEHI beneficiaries in Nagasaki Prefecture, regardless of whether or not they were prescribed any drugs.

Statistical analysis. We calculated the characteristics of the insured persons prescribed drugs, including their age, the number of drugs used, the pharmacy fee (Japanese yen), and the pharmaceutical fee (Japanese yen) (110 yen = 1 US dollar as of June 20, 2018) according to the patient's polypharmacy status. A chi-square test and *t*-test were used for categorical and continuous variables, respectively, based on differences in polypharmacy status. We calculated the numbers and percentages of persons in the different age groups among those aged ≥65 years with polypharmacy, by sex. *P*-values <0.05 were considered statistically significant.

All statistical analyses were performed using EZR (ver. 1.36; Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, EZR is a modified version of R commander, designed to add the statistical functions frequently used in biostatistics [17].

Results

The number of individuals prescribed one or more drugs at least once during the study period was 379,988 (225,668 in the NHI and 154,320 in the LEHI), accounting for 62.8% of all NHI and LEHI beneficiaries as of April 2016. For those aged ≥65 years, 78.1% of the residents in Nagasaki Prefecture were prescribed one or more drugs at least once during the study period. The age distributions of the insured persons (n = 605,406) and the persons with prescriptions (n = 379,988) are shown in Table 1.

Table 2 summarizes the characteristics of the persons with prescriptions according to their polypharmacy status. The mean age of the persons with prescriptions was 70.3 years, and 41.8% of these persons were male. The median number of drugs prescribed

Table 1 Age distributions of the persons with insurance and those with prescriptions

	Persons with prescriptions	Persons with insurance
Participation rate by age group		
0–9 years (%, n)	2.7 (10,429)	3.3 (19,819)
10–19 years (%, n)	2.2 (8,385)	4.1 (24,745)
20–29 years (%, n)	1.9 (7,120)	4.0 (24,186)
30–39 years (%, n)	2.6 (9,940)	5.1 (30,577)
40–49 years (%, n)	3.6 (13,760)	6.4 (38,533)
50–59 years (%, n)	5.5 (20,961)	8.5 (51,181)
60–69 years (%, n)	21.2 (80,401)	23.3 (141,026)
70–79 years (%, n)	29.2 (110,978)	22.8 (138,184)
80–89 years (%, n)	24.5 (92,952)	18.0 (108,832)
≥90 years (%, n)	6.6 (25,062)	4.7 (28,323)
Total	100 (379,988)	100 (605,406)
Male sex (%)	41.8	45.5

Data are the mean ± standard deviation (SD), percentage and number, or median and interquartile range, as appropriate.

was 3.7 per patient, ranging from 1.7 to 7.0. The pharmacy and pharmaceutical fees, per patient, were 6,600 yen and 25,590 yen, respectively. Overall, 121,033 (31.9%) persons had polypharmacy status. The persons with polypharmacy were significantly more likely to be female ($p<0.001$), older ($p<0.001$), with a higher pharmacy fee ($p<0.001$) and a higher pharmaceutical fee score ($p<0.001$).

Table 3 indicates the numbers of patients in the different age groups among those aged ≥65 years with polypharmacy, by sex. In total, 121,033 persons engaged in polypharmacy (45,629 males and 75,404 females), of which 110,538 with polypharmacy were aged ≥65 years.

Table 4 provides the percentages of persons with prescriptions and insured persons with polypharmacy, by age and sex. Among the persons with prescriptions, the percentage of those with polypharmacy increased

Table 2 Characteristics of persons with prescriptions according to polypharmacy status

	Persons with prescriptions	Polypharmacy		
		(−) (N = 258,955)	(+) (N = 121,033)	*p*-value
Age (years)	70.3 (19.3)	65.8 (20.6)	79.2 (12.4)	< 0.001
Male sex (%)	41.8	43.5	37.7	< 0.001
Number of drugs	3.7 (1.7–7.0)	2.5 (1.6)	10.2 (3.9)	< 0.001
Pharmacy fee (yen)	6,600 (2,100–13,500)	1,100 (380–2,250)	5,600 (4,250–7,500)	< 0.001
Pharmaceutical fee (yen)	25,570 (6,370–72,240)	3,920 (1,120–10,600)	31,000 (17,660–54,410)	< 0.001

Data are the mean ± SD, percentage and number, or median and interquartile range, as appropriate.

Table 3 Classification of persons with polypharmacy aged ≥65 years according to age group and sex

	Number of persons with polypharmacy		
Age	Total	Males	Females
65–69 years	9,760	4,810	4,950
70–74 years	14,272	6,414	7,858
75–79 years	23,298	9,139	14,159
80–84 years	26,901	9,973	16,928
85–89 years	21,661	6,838	14,823
≥90 years	14,646	3,387	11,259
Total number of persons aged ≥65 years	110,538	40,561	69,977
Total number of persons	121,033	45,629	75,404

Table 4 Percentage of persons with polypharmacy aged ≥65 years according to age group and sex

	Persons with prescriptions			Persons with insurance		
Age	Total	Males	Females	Total	Males	Females
65–69 years (%)	17.8	19.0	16.9	11.1	11.5	10.8
70–74 years (%)	28.5	28.8	28.3	22.2	22.4	22.0
75–79 years (%)	38.3	36.2	39.7	31.6	29.6	33.0
80–84 years (%)	49.2	46.1	51.2	41.4	39.7	42.4
85–89 years (%)	56.6	53.1	58.4	49.4	48.8	49.8
≥90 years (%)	58.5	64.6	59.1	51.7	62.8	50.9
% of total persons aged ≥65 years	39.0	35.8	31.5	30.5	27.7	32.3
% of total persons	31.8	28.8	34.0	20.0	16.9	22.4

Data are expressed as percentages.

with age, with 31.8% engaged in polypharmacy overall (28.8% males and 34.0% females). In particular, about 40% of those aged ≥ 65 years engaged in polypharmacy. Among the insured persons, similar results were obtained, with 20.0% engaged in polypharmacy, 30.5% of whom were aged ≥ 65 years.

In summary, approximately one-third of the persons with prescriptions engaged in polypharmacy, with approximately one-fifth of insured persons engaged in polypharmacy. Among those aged ≥ 65 years, the polypharmacy rate was high at 39% of the persons with prescriptions and 30% of the insured. Among those aged > 85 years, about half engaged in polypharmacy.

Discussion

Our analyses clarified the prevalence of polypharmacy among the beneficiaries of the NHI and LEHI in Nagasaki Prefecture, Japan. About one-fifth of the beneficiaries of the NHI and LEHI engaged in polypharmacy, and this was especially prevalent among those aged > 85 years, half of whom engaged in polypharmacy.

There are several reasons for this large number of elderly people engaging in polypharmacy. In Japan, most older patients tend to receive fragmented and overlapping medical services from multiple medical institutions [8]. The medical records of patients are usually created per facility, with no opportunity to confirm the existence of a patient's medical records from one facility to the other. A similar situation has been recognized with pharmacies. The pharmaceutical dispensing history in one pharmacy in Japan cannot be confirmed in another pharmacy. To improve this situation, the use of only one "family pharmacy" has been recommended with which the entire history of an individual from both the medical institution(s) and pharmacies can be accurately and continuously monitored for each individual. Pharmaceutical management, guidance, and medication histories can also be monitored accurately with the use of the single family pharmacy, and all historical records can then be consolidated [18].

However, only 20% of patients were familiar with the concept of a family pharmacy [19]. Considering this, many patients used 2 or more pharmacies, thereby making it difficult to ascertain how many drugs each patient has taken. As a result, the numbers of drugs taken by patients are likely to increase [20]. Family physicians also play an important role in solving this issue [7]. It is the responsibility not only of the family pharmacy but also the family physician to determine how many drugs each patient takes. The family physician must also manage patients' prescriptions while considering the health care goals and activity level of each patient.

Few studies have discussed the polypharmacy status in a population-representative situation. In a study of 660 patients who visited one of the geriatric outpatient units of five university hospitals, the average number of drugs taken was 4.4 [8]. Another observational study indicated that among patients hospitalized for geriatric internal medical care, the average numbers of drugs taken for cases without and with adverse events during hospitalization were 5.0 ± 3.6 and 5.7 ± 4.1, respectively [21]. However, since the prior studies of polypharmacy were limited to patients in specific medical institutions, the polypharmacy status in a population-representative situation has not been established. Our present findings revealed this status by using the HICs data of about 370,000 individuals who were prescribed drugs and the data of beneficiaries without prescribed drugs during the study period.

The average number of drugs prescribed in our study population was 3.7, and about half of the patients aged > 80 years were using 6 or more drugs. In another study, the higher average number of drugs reported was not consistent with our present results. We suspect that the previous results were obtained because the target population was comprised of individuals from geriatric outpatient units and thus may not represent the total population. The strengths of our present investigation lie in the characteristics of the study population, which included all patients aged ≥ 75 years within the prefecture as well as patients who did not receive prescriptions during the follow-up. Thus, our results showing that the state of polypharmacy in this population-representative situation was much higher than expected, especially among elderly people, may be generalized.

In elderly people, adverse drug events — which tend to occur frequently — may be associated with polypharmacy due to their aging and to a reduction in kidney and/or liver functions. In Japan, > 10% of hospitalized patients are reported to experience adverse drug events [8]. It has been reported that 88% of hospital admissions due to adverse drug events in elderly people, are

preventable, and that the number of cases can be sevenfold higher in older than in younger individuals [22]. According to Fried *et al.* [23], it is important to carefully consider the benefits and risks involved in drug selection strategies as well as strategies to reduce the drug intakes of elderly people. The Screening Tool Of Older Person's Prescriptions and the Screening Tool To Alert Doctors to the Right Treatment criteria as well as the Beers Criteria have been proposed in Europe and the United States, and they have been used in the selection of drugs for elderly people [24, 25].

In 2015, the Japan Gerontological Society announced the 'Guidelines for Medical Treatment and Its Safety in Elderly People 2015,' which recommended that prescriptions for individuals aged ≥ 75 years and those aged < 75 years with frailty or under nursing care be reviewed [7]. Because the risk-benefit trade-offs of managing medications in older patients is a complicated problem, the use of these guidelines is said to be of benefit [26]. In our present study, drugs that should not be administered based on these guidelines were not investigated. Considering the high prevalence of polypharmacy among elderly people, future studies should investigate the association between polypharmacy and prognoses.

Notably, this study has three major strengths. The first is that it included data from multiple family and hospital pharmacies. In Japan, the pharmaceutical dispensing history in one pharmacy cannot be confirmed by another pharmacy. We therefore used HIC data in this study, which means that even if patients used multiple pharmacies, it was possible to include all of the information about their prescribed drugs under their health insurance package. The second major strength of this study was that, by using HIC data, even if there was a change from the NHI to LEHI insurance coverage, the transfer of patient information from one agency to another is possible. A study using the Diagnosis Procedure Combination data [16] could not detect the situation in which the subject changed insurance coverage within the analyzed period. Under the current system, generally, patients are supposed to automatically begin to participate in the LEHI on their 75th birthdays, but even if the patients withdraw from the NHI and move to LEHI, their data (*e.g.*, personal information) are not connected. Since we used HIC data and the qualification status information from both the NHI and the LEHI, even if any patient changed insurance coverage within the analyzed period, there was no data loss.

The third major strength of this study was our evaluation of the patients' data covering 3 consecutive months, including cases with long-term prescriptions. In Japan, the average interval since the last outpatient visit has increased [27]. Moreover, the limitation of the lengths of drug prescriptions was cancelled in 2002, with exceptions for some special medications. According to a questionnaire conducted by the Japan Medical Association, the average interval since the last outpatient visit among patients with chronic diseases such as hypertension and dyslipidemia was ≥ 8 weeks for approximately half of the patients <Japan Medical Association, URL: http://www.med.or.jp/etc/eq201103/hoken/110311eq140.pdf>. In our study, we evaluated an interval of 3 consecutive months, and it was thus possible to evaluate all data (even the long-term [> 8-week] prescriptions).

There are also several limitations to our study, most of which are related to the use of HIC data. First, we did not directly investigate the specific prescription situations; we only obtained the available HIC information. Since there was no information regarding over-the-counter drugs not covered by the health insurance system, our results could have underestimated the number of drugs used by older patients. However, under the Japanese universal healthcare insurance system, it is possible to obtain all of the information about drugs covered by the health insurance system from the HIC data. There is a need for further studies that include over-the-counter drugs not covered by the health insurance.

Secondly, it is possible that this study underestimated the number of drugs prescribed per month. Even if the period between visits was the same, there might have been 2 patterns: (1) the first visit was before April and the second visit was between April and June, and (2) both the first and second visits were between April and June. It is also possible that the number of drugs prescribed per month may have varied during the study period, even though the interval between patient visits was the same. The actual number of drugs prescribed per month may have been greater than the value obtained in this study. However, this does not affect the interpretation of the results substantially. Future studies should investigate the mean daily number of medications taken by patients determine more precisely the actual polypharmacy status.

Thirdly, we did not have information on the types or amounts of drugs prescribed and did not analyze the differences between regularly prescribed drugs and temporary drugs. Further analyses considering this difference between regularly prescribed drugs and medicines to be taken as needed are desirable. Fourth, our study population was limited to beneficiaries of the NHI and LEHI. However, we investigated all of the people aged ≥75 years in Nagasaki Prefecture because the LEHI covers all of the residents aged ≥75 years within the prefecture. Fifth, we could not confirm whether the patients' prescriptions were appropriate. All drugs have potential benefits as well as risks, and the trade-off between the benefits and risks is difficult to quantify. Similarly, a relationship between polypharmacy and under-prescription has been reported; the probability of under-prescription increased significantly with the number of medicines being used [28,29]. Under-prescription may be an important aspect of inappropriate prescribing for individuals with polypharmacy. Under-prescription can also put a patient at risk for disease, such as cardiovascular diseases [30]. Future studies should investigate both the prevalence of non-recommended drug use/under-prescription based on the relevant guidelines and the association between polypharmacy and the risk of adverse drug reactions as well as health outcomes by using large-scale population-based data.

Lastly, a distinguishing feature of Nagasaki Prefecture is the number of islands included in the prefecture. One of the prefecture that has the largest number of islands with inhabitants in Japan, Nagasaki Prefecture is comprised of approximately 73 islands. While the population of residents of the islands is approximately 10% of the total Nagasaki population, most people who live on the islands are older, and because of limited medical facilities on the islands, medical care is often limited. Consequently, these elderly residents are more likely be prescribed multiple medications per medical visit. This potential for over-prescribing may have affected our results [31].

In conclusion, we used the HIC data from a large-scale population-based database to investigate the number of elderly patients with polypharmacy. Our analyses demonstrated that about one-third of the elderly people had polypharmacy status, and about half of the people aged >85 years had polypharmacy status. These results showed that the number of elderly people with polypharmacy in population-representative settings might be much higher than previously described.

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