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The role of mental disease on the association between multimorbidity and medical expenditure

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Running title

Medical expenditure, multimorbidity, and mental disease

Keywords

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Key messages

- Multimorbidity was associated with high medical expenditure in Japan.
- Mental diseases had a significant interaction effect on this association.
- Mental diseases are comorbidities that may contribute to increased medical costs.

ABSTRACT

Background. Multimorbidity is the presence of two or more chronic diseases and is associated with increased adverse outcomes, including hospitalization, mortality, and frequency of use of medical institutions.

Objective. This study aimed to describe multimorbidity patterns, determine if multimorbidity was associated with high medical expenditure, and determine whether mental diseases had an interaction effect on this association.

Methods. We conducted a claims data-based observational study. Data were obtained for 7,526 individuals aged 0–75 years from a medical claims dataset for Goto, Japan, over a 12-month period (2016–2017). Annual medical expenditure was divided into quintiles; the 5th quintile represented high medical expenditure. Multimorbidity status was defined as the occurrence of two or more health conditions from 17 specified conditions. Odds ratios (OR) and 95% confidence intervals (CI) for high medical expenditure were calculated by number of comorbidities.

Results. In total, 5,423 (72.1%) participants had multimorbidity. Multimorbidity was significantly associated with high medical expenditure, even after adjustment for age, sex and income category (OR 10.36, 95% CI: 7.57–14.19; $P < 0.001$). Mental diseases had a significant interaction effect on the association between multimorbidity and high medical expenditure ($P = 0.001$).

Conclusions. Multimorbidity is associated with high medical expenditure in Japan. Mental diseases may contribute to increased medical costs.

Introduction

In the context of population aging and advances in medical care and public health policy, disease structure has changed from single diseases to multiple coexisting diseases, generally referred to as multimorbidity (1). Consequently, physicians have had to adopt a comprehensive approach to treat multimorbidities (2). Multimorbidity is the co-occurrence of two or more chronic diseases such as hypertension, dyslipidemia, and bronchial asthma (3). The proportion of comorbidities increases with age, with about 75% multimorbidity at age 70 years in primary care settings (1).

Recent studies have shown associations between multimorbidity and hospitalization, mortality, frequency of use of medical institutions, and physical function decline (4, 5). It has also been reported that the number of drugs prescribed and medical costs would increase if physicians followed the drug recommendations in various disease management guidelines (2). In addition, single-disease management guidelines are not always effective for populations with a high rate of multiple comorbidities. A growing number of studies have reported an association between multimorbidity and high medical costs (4, 6, 7). Therefore, multimorbidity is an important issue at both individual care and medical system levels.

There is a paucity of studies investigating specific multimorbidity patterns associated with high medical expenditure (4, 6, 7). Mental diseases are known risk factors for poor medication adherence and healthcare utilization (8–10). The present study aimed to describe the multimorbidity pattern in Goto city, Japan, and determine if multimorbidity was associated with high medical expenditure. In addition, we aimed to clarify if there was an interaction effect of mental diseases on this association.

Methods

The Japanese healthcare system

Japan has provided universal health coverage since 1961 (11). Japanese health insurance systems are based on employment patterns: (1) Kokuho insurance (citizens' health insurance) is mainly for farmers, other self-employed workers, and retired workers and their families, (2) government-managed health insurance is for workers in small firms, (3) society-managed health insurance covers workers in large companies and industry sectors, (4) mutual aid associations are available for some public-sector employees, and (5) the medical care system covers older senior citizens (residents aged

≥75 years). This range of social medical insurance ensures that almost all individuals are insured and have to pay only 20%–30% of their total medical expenditure as out-of-pocket payments. However, if the monthly copayment exceeds a specified amount, beneficiaries can apply for a high-cost medical expense benefit, which reduces the copayment to 1%.

Japan has therefore achieved universal health coverage and is known for its good health outcomes. However, owing to a scarcity of gatekeepers (e.g., primary care physicians) patients can self-refer to secondary care or tertiary care hospitals (12). Physicians in Japan are free to advertise and practice any specialty they wish and national quotas for training do not exist, which has led to too many subspecialists compared with primary care physicians (13).

In 2000, the Japanese government initiated mandatory public long-term care insurance (LTCI) to help older people lead more independent lives and relieve the burden on family caregivers. The municipal government has provided long-term care services for community-dwelling adults aged 65 years or older who experience difficulties at home (e.g., individuals who are bedridden or have dementia) and are certified as care recipients by a committee based on the LTCI Act. The LTCI application process has been described elsewhere (14).

Setting and Participants

We conducted this study in Goto city, western Japan. Goto is situated on a remote, rural archipelago off the coast of Nagasaki prefecture. In 2015, the population of Goto city was 37,327; a large proportion of residents were aged ≥65 years (36.8%).

In Goto city, there are 4 hospitals (2 public and 2 private), 41 clinics, 10 facilities covered by LTCI, 4 home-visit nursing services, 23 group homes for older adults with dementia, and 25 geriatric facilities not covered by LTCI. The largest public hospital (304 bed capacity) is a single facility providing psychiatric care. Most acute diseases are referred to this hospital, although hemorrhagic stroke cases or cases requiring cardiovascular surgery are transferred to the mainland using emergency helicopters.

The Goto Municipal Government has stored claims data since March 2016 using the Kokuho-Database System (a medical claim analysis system). Claims are recorded for beneficiaries of national health insurance societies aged 0–75 years. Information on all

medical claims made by beneficiaries is collected monthly by the Goto Municipal Government.

We used data from the medical claims dataset for beneficiaries' age, sex, address, claims for outpatient and/or inpatient care during the study period, income category, medical expenditure, and diagnosis codes using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Income category was defined as low (an inhabitant tax-exempt household), middle (a household with normal taxable income; e.g. annual household income less than 6,000,000 Japanese yen [¥], equivalent to 58,252 US dollars [$], for those aged <70 years old), or high (a household with high taxable income; e.g. annual household income over ¥6,000,000 for those aged <70 years old) (the mean exchange rate on September 1, 2016, was ¥103 to $1).

Study design

All analyses were based on claims data of beneficiaries of national health insurance societies. We used data for 72,082 claims made in the study period (between September 2016 and August 2017). We excluded cases with missing data in the medical claims dataset.

We cooperated with the Goto Municipal Government Division of Public Health to analyze data from the Kokuho-Database System. However, we could not access the other four types of social insurance system as they are separately managed by each insurer.

Multimorbidity definition

There are many definitions of multimorbidity (1). As we focused on the medical costs and additive effect of mental diseases, definitions of specific health conditions and their combinations were essential. Therefore, following previous studies, we used the ICD-10 coded specified health conditions rather than simple sum of patient self-reported health conditions (15, 16).

Multimorbidity was defined as the co-occurrence of two or more comorbidities from 17 health conditions: hypertension (ICD-10 codes I10–15, O10–16), diabetes (E10–14), dyslipidemia (E15–90), stroke (I60, 61, 63, 69), cardiac diseases (I01–20, 27, 30–52, Q20–24; e.g., coronary heart disease, heart failure, arrhythmia), chronic respiratory

diseases (J7–11, 19, 22–29, 31–39, 41–99; e.g., asthma, chronic obstructive pulmonary disease), digestive diseases (K25–27, 29; e.g., gastroesophageal reflux disease, cirrhosis), kidney diseases (N00–17, 19; e.g., chronic kidney disease), urologic diseases (N25–40, 99; e.g., prostatic hypertrophy, overactive bladder), arthritis or rheumatism (M05–19, 53, 54, 75; e.g., osteoarthritis, rheumatoid arthritis), lumbar diseases (M40–43, 45–51, 53, 54; e.g., lumbar spinal stenosis, osteoporosis), neurologic diseases (G00–99; e.g., epilepsy, dementia), mental disorders (F00, 02, 04–48, 49–99; e.g., depression), endocrine diseases (E00–07, 15–90; e.g., thyroid disorders), malignancy (C00–97), vision abnormalities (H25, 26, 52), and skin diseases (L10–14, 20–30, 40–98; e.g., atopic dermatitis) (15, 17).

We examined each patient's entire medical claims data during the 12-month study period. If any above-mentioned ICD-10-coded health condition was reported at least once during the study period, we counted it as one health condition. If duplicated health conditions were reported more than once, we regard these as one health condition (e.g., if the data for a patient with hypertension reported code I10 12 times in separate claims, we counted these as one health condition).

All ICD-10-coded diagnoses were listed and used to define multimorbidity. We categorized the number of comorbidities into four groups: 0–1, 2–3, 4–5, and ≥6 comorbidities.

Medical expenditure

Every time a patient visits a medical facility, the facility must report medical claims data to social insurers to be reimbursed. As the Japanese government regulates medical costs, including drugs and dentistry, to the same level for all social insurers, medical facilities cannot charge higher prices. We obtained all healthcare costs for each patient from monthly medical claims data. Annual total expenditure was calculated as the sum of monthly medical expenditure. This was divided into quintiles. The 5th quintile was defined as the highest category of medical expenditure, as there is no consensus in the literature on the threshold proportion of high annual medical expenditure (18). Expenditures are presented as both Japanese yen and US dollars (the mean exchange rate on September 1, 2016, was ¥103 to $1).

Statistical analysis

First, we performed univariable logistic regression analysis. Next, we used multivariable logistic regression analysis to determine the relationship between comorbidity and high medical expenditure. In the multivariable model, we adjusted for age and sex as a priori confounding factors. We also evaluated the interaction effect of mental diseases on the association between multimorbidity and medical expenditure. We performed a sensitivity analysis of these associations using different multimorbidity cutoff points (≥3 or ≥4 comorbidities). All P-values for statistical tests were two-tailed; values of <0.05 were regarded as statistically significant. Statistical analyses were performed using STATA® version 14.0 (StataCorp, College Station, TX, USA).

Ethics Statement

This study followed the principles of the Declaration of Helsinki. Ethical approval for the study was obtained in accordance with local institutional requirements (Nagasaki University, Japan, project registration number: 18033040).

Results

Of 72,082 claims cases, 0.9% (648cases) had missing ICD-10 codes or income category, so these data could not be included in the analyses. Finally, data for 7,526 participants (accounting for 71,434 claims cases) were analyzed. **Table 1** shows participant characteristics. The median age was 62 years, 48% were male, and 921 (12.2%) had a hospital admission during the 12-month study period. In total, 5,423 (72.1%) participants had multimorbidity. The annual medical expenditure was 630–14,631,200 Japanese yen (6–142,050 US dollars) per year. The maximum medical expenditure in the highest quintile was 600 times higher than that in the lowest quintile.

The univariate analysis identified the following factors significantly associated with high medical expenditure: age, male sex, admission during the study period, income category, hypertension, diabetes, dyslipidemia, stroke, cardiac diseases, digestive diseases, kidney diseases, urologic diseases, arthritis or rheumatism, lumbar diseases, neurologic diseases, mental disorders, endocrine diseases, malignancy, vision abnormalities, and skin diseases (**Table 2**). Multimorbidity (≥2 comorbidities) was significantly associated with high medical expenditure (odds ratio [OR] 13.86, 95%

confidence interval [CI]: 10.51–18.28; P < 0.001). This remained significantly after adjustment for age, sex and income category (OR 10.58, 95% CI: 7.99–14.01; P < 0.001).

Next, we tested the OR and 95% CI for high medical expenditure in relation to the interaction between multimorbidity and mental diseases (**Table 3**). Mental diseases had a significant interaction effect on the association between multimorbidity and high medical expenditure (P = 0.001).

A sensitivity analysis showed that multimorbidity (≥3 or ≥4 comorbidities) was significantly associated with high medical expenditure (OR 11.65, 95% CI: 9.63–14.09; P < 0.001, OR 9.23, 95% CI: 7.97–10.69; P < 0.001, respectively) (**Supplementary Table 1**). Mental diseases had a significant interaction effect on the association between multimorbidity (≥3 or ≥4 comorbidities) and high medical expenditure (P < 0.001, P < 0.001, respectively) (**Supplementary Table 2**).

Figure 1 shows the ORs for high medical expenditure stratified by number of comorbidities (0–1, 2–3, 4–5, ≥6) and comorbid mental diseases (No, Yes). We treated participants with 0–1 comorbidities and no comorbid mental diseases as the reference group. ORs for those without comorbid mental diseases increased as the number of comorbidities increased (1, 3.9, 11.8, and 42.7 for 0–1, 2–3, 4–5, and ≥6 comorbidities, respectively). The ORs for comorbid mental diseases also increased as the number of comorbidities increased (8.2, 11.3, 21.7, and 66.3 for 0–1, 2–3, 4–5, and ≥6 comorbidities, respectively).

Discussion

We found that among the beneficiaries of national health insurance societies in Goto city, Japan, medical costs increased as the number of comorbidities increased. This is consistent with the results of previous research conducted in Japan, Spain, and Switzerland (16, 19, 20). A possible explanation for the association between multimorbidity and high medical expenditure is that patients with multimorbidity may receive more home care visits or visit emergency departments more frequently, although we did not investigate this. One Japanese community-based observational

study showed that multimorbidity (defined by Charlson Comorbidity Index score) was associated with LTCI requirement after adjusting for age, sex, and household income (16). This suggests that older Japanese people with multimorbidity tend to receive more social welfare services such as home care visits or nursing care. A cross-sectional study of French nursing home residents showed that multimorbidity was associated with emergency department visits (OR 1.79; 95% CI: 1.24–2.58) (21).

An important finding of this study was that comorbid mental diseases had an additive effect on the high medical costs associated with an increased number of comorbidities. Public health strategies in Japan have focused on early detection of lifestyle-related diseases such as cardiovascular diseases and cancers. Our findings suggest that public health strategies should also focus on mental diseases to constrain overall medical expenditure at the community level.

The mental disease subcategory used here included mood disorders (e.g., major depression), somatoform disorder, and intellectual disabilities. Depression is a major comorbid disease in individuals with cardiovascular diseases, and increases healthcare use and poor medication adherence (8–10), factors which may have contributed to the interaction effect of mental diseases on the association between multimorbidity and high medical expenditure among our participants.

It is also possible that participants with mental diseases are less likely to undergo screening for cardiovascular diseases or cancers than those without mental diseases. Since 1982, the Goto Municipal Government has promoted medical examinations for community-dwelling adults aged ≥40 years for screening and treating non-communicable diseases under the Health and Welfare for the Aged Act. The municipal government provides these annual medical check-ups at community centers in all districts and small islands in Goto city. However, individuals with mental diseases tend to participate less in these check-ups than those without mental diseases.

Application to family practice

The study highlights two aspects of the clinical management of multimorbidity. First, family physicians can recognize and coordinate medical service use among multimorbid

patients with mental diseases. Multimorbidity needs a holistic and comprehensive approach to recognize polypharmacy; to screen frailty using comprehensive geriatric assessment; to assess health problems that affect quality of life; and to establish patient goals, values, and priorities (22). A recent guideline suggests that physicians should be alert to the possibility of depression and anxiety, as common mental diseases are constituents of multimorbidity (22). Although clinical practice mainly focuses on identifying, assessing, and managing mental conditions in multimorbid patients, our findings highlight the value of considering the high medical expenditure of multimorbidity.

Second, family physicians can easily provide holistic and comprehensive care, which may help to reduce the high medical expenditure owing to acute illness among comorbid people with mental diseases. Starfield suggests that "it is not chronicity *per se* that creates a burden on the health-care system" ... many non-chronic conditions behave as if they were chronic – persisting or recurring over time" (23). Thus, chronic illnesses among multimorbid individuals predispose to acute illnesses. Therefore, comprehensive care and continuity of care by family physicians could help to identify vulnerable multimorbid individuals, and to balance and optimize chronic and acute illness care.

Study limitations

Some study limitations should be mentioned. First, although we used patient age, sex and income category as confounders, the retrospective data collection did not permit the assessment of potential confounders of other socioeconomic status (e.g., years of education) (15, 16, 24). Second, we were unable to establish cause–effect relationships as this was a cross-sectional study. Differences in measures of exposure, outcomes, and potential confounders might have affected the results. Third, we used medical claims data from national health insurance societies; these data may include inaccuracies in the ICD-10-coded diagnoses. However, several studies have shown high positive predictive values of cardiovascular diseases using hospital-based ICD-10-coded diagnoses (25, 26). Fourth, this study was conducted on remote Japanese islands, which may affect the generalizability of the findings. However, geographic island boundaries may strengthen the comprehensiveness of healthcare service use within the islands, which may have clarified the association between variables. Fifth, we had access only to Kokuho

insurance data. The lack of data on older citizens aged ≥75 years may have biased the results, because older patients usually have multimorbidity and require higher healthcare costs. And there is an overlap in some healthcare services (e.g., home care visits and home nursing care) between medical insurance and LTCI in Japan. A prospective study including participants aged ≥75 years, and collecting data on medical expenditure and LTCI use is needed.

In conclusion, multimorbidity is gaining importance and represents an economic burden for the community. Our findings show that multimorbidity is associated with high medical expenditure in Japan. Mental diseases are comorbidities that may increase medical costs.

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Conflict of interest

All authors declare no conflicts of interest.

Ethical approval

This study followed the principles of the Declaration of Helsinki. Ethical approval for this study was obtained in accordance with local institutional requirements (Nagasaki University, Japan; project registration number: 18033040).

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Tables

Table 1. Characteristics of 7,526 participants aged 0–75 years from a medical claims dataset for Goto, Japan, over a 12-month period (2016–2017).

Variables	Number (%)
Medical care claim records	714,34
Study sample	7,526
Male	3,607 (47.9)
Median age (25th, 75th percentile)	62 (47, 67)
Admission during the study period (≥1)	921 (12.2)
Income category	
High	157 (2.1)
Middle	4,542 (60.4)
Low	2,827 (37.6)
Comorbidity	
Hypertension	2,765 (36.7)
Diabetes	1,367 (18.2)
Dyslipidemia	2,416 (32.1)
Stroke	317 (4.2)
Cardiac diseases	1,230 (16.3)
Chronic respiratory diseases	1,584 (21.1)
Digestive diseases	2,643 (35.1)
Kidney diseases	224 (3.0)
Urologic diseases	684 (9.1)
Arthritis and rheumatism	2,336 (31.0)
Lumbar diseases	1,093 (14.5)
Neurologic diseases	1,903 (25.3)
Mental disorders	1,104 (14.7)
Endocrine diseases	2,600 (34.6)
Malignancy	586 (7.8)
Vision abnormalities	1,748 (23.2)

Skin diseases	2,063 (27.4)
Number of comorbidities	
0–1	2,103 (27.9)
2–3	2,009 (26.7)
4–5	1,671 (22.2)
≥6	1,743 (23.2)
Multimorbidity (≥2 comorbidities)	5,423 (72.1)
Annual medical expenditure	
1st quintile	¥630–23,900 ($6–232)
2nd quintile	¥23,930–73,490 ($232–713)
3rd quintile	¥73,600–153,650 ($715–1,492)
4th quintile	¥153,700–324,780 ($1,492–3,153)
5th quintile	¥324,960–14,631,200 ($3,155–142,050)
High medical expenditure	1,505 (20.0)

¥103 was equivalent to $1, which was the exchange rate on September 1, 2016.

Table 2. Odds ratios and 95% confidence intervals for factors related to high medical expenditure (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

Variable	High medical expenditure		
	OR	95% CI	P
Age (years)	1.04	(1.03–1.04)	<0.001
Sex (male)	1.32	(1.18–1.48)	<0.001
Admission during the study period (≥1)	34.58	(28.79–41.54)	<0.001
Income category	1.40	(1.26–1.57)	<0.001

Comorbidity			
Hypertension	2.74	(2.45–3.08)	<0.001
Diabetes	3.59	(3.16–4.08)	<0.001
Dyslipidemia	2.84	(2.53–3.19)	<0.001
Stroke	4.82	(3.84–6.06)	<0.001
Cardiac diseases	4.15	(3.64–4.74)	<0.001
Chronic respiratory diseases	2.32	(2.05–2.63)	<0.001
Digestive diseases	3.55	(3.16–3.99)	<0.001
Kidney diseases	8.53	(6.43–11.32)	<0.001
Urologic diseases	3.22	(2.73–3.80)	<0.001
Arthritis and rheumatism	3.40	(3.02–3.82)	<0.001
Lumbar diseases	2.81	(2.45–3.23)	<0.001
Neurologic diseases	4.39	(3.89–4.94)	<0.001
Mental disorders	3.08	(2.68–3.54)	<0.001
Endocrine diseases	2.90	(2.59–3.26)	<0.001
Malignancy	5.23	(4.40–6.22)	<0.001
Vision abnormalities	1.91	(1.69–2.16)	<0.001
Skin diseases	1.43	(1.27–1.62)	<0.001
Number of comorbidities			
0–1	Ref		
2–3	3.99	(2.92–5.45)	<0.001
4–5	10.98	(8.06–14.95)	<0.001
≥6	39.14	(27.72–55.26)	<0.001
Multimorbidity	13.86	(10.51–18.28)	<0.001

OR, odds ratio; CI, confidence interval.

Table 3. Odds ratios and 95% confidence intervals for high medical expenditure in relation to multimorbidity (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

	OR	95% CI	P

Age	1.03	(1.02–1.03)	<0.001
Sex	1.43	(1.27–1.61)	<0.001
Income category	1.29	(1.15–1.45)	<0.001
Multimorbidity	10.36	(7.57–14.19)	<0.001
Mental diseases	7.98	(3.89–16.36)	<0.001
Interaction between number of comorbidities and mental diseases	0.30	(0.14–0.62)	0.001

OR, odds ratio; CI, confidence interval

Supplementary Table 1. Odds ratios and 95% confidence intervals for factors related to high medical expenditure by different multimorbidity cutoff points (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

OR, odds ratio; CI, confidence interval.

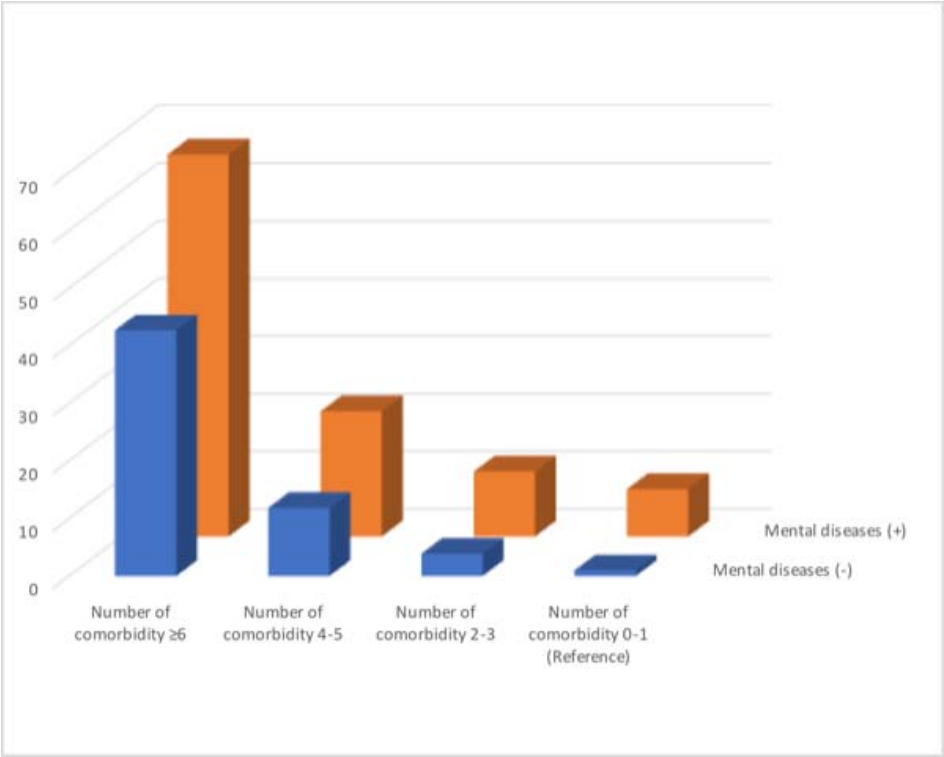
Supplementary Table 2. Odds ratios and 95% confidence intervals for high medical expenditure in relation to multimorbidity by different multimorbidity cutoff points (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

OR, odds ratio; CI, confidence interval.

Figures

Figure 1. Odds ratios for high medical expenditure in relation to multimorbidity and mental diseases (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

Figure 1.


70
60
50
40
30
20
10
0
Number of comorbidity ≥6
Number of comorbidity 4-5
Number of comorbidity 2-3
Number of comorbidity 0-1 (Reference)
Mental diseases (+)
Mental diseases (-)

Supplementary Table 1. Odds ratios and 95% confidence intervals for factors related to high medical expenditure by different multimorbidity cutoff points (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

Variable	High medical expenditure		
	OR	95% CI	P
Number of comorbidities			
0–2 (N = 3,202)	Ref		
3–5 (N = 2,581)	5.91	(4.78–7.29)	<0.001
≥6 (N = 1,743)	25.60	(20.06–32.67)	<0.001
Multimorbidity (≥3 comorbidities)	11.65	(9.63–14.09)	<0.001
Number of comorbidities			
0–3 (N = 4,112)	Ref		
4–5 (N = 1,671)	4.57	(3.82–5.46)	<0.001
≥6 (N = 1,743)	16.28	(13.51–19.62)	<0.001
Multimorbidity (≥4 comorbidities)	9.23	(7.97–10.69)	<0.001

OR, odds ratio; CI, confidence interval.

Supplementary Table 2. Odds ratios and 95% confidence intervals for high medical expenditure in relation to multimorbidity by different multimorbidity cutoff points (N = 7,526, derived from a medical claims dataset for Goto, Japan, over a 12-month period, 2016–2017).

	OR	95% CI	P
Multimorbidity (≥3 comorbidities)			
Age	1.02	(1.01–1.02)	<0.001
Sex	1.45	(1.28–1.64)	<0.001
Income category	1.30	(1.15–1.46)	<0.001
Multimorbidity	10.02	(7.97–12.61)	<0.001
Mental diseases	5.31	(3.46–8.15)	<0.001
Interaction between number of comorbidities and mental diseases	0.40	(0.25–0.63)	<0.001
Multimorbidity (≥4 comorbidities)			
Age	1.01	(1.01–1.02)	<0.001
Sex	1.39	(1.23–1.58)	<0.001
Income category	1.26	(1.12–1.43)	<0.001
Multimorbidity	8.38	(6.98–10.05)	<0.001
Mental diseases	4.55	(3.35–6.19)	<0.001
Interaction between number of comorbidities and mental diseases	0.43	(0.30–0.60)	<0.001

OR, odds ratio; CI, confidence interval.