

# Physical multimorbidity patterns and depressive symptoms: a nationwide cross-sectional study in Japan

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**To cite:** Aoki T, Yamamoto Y, Shimizu S, *et al.* Physical multimorbidity patterns and depressive symptoms: a nationwide cross-sectional study in Japan. *Fam Med Com Health* 2020;**8**:e000234. doi:10.1136/fmch-2019-000234

## ABSTRACT

**Objective** The associations of physical multimorbidity with depressive symptoms have been investigated in a number of studies. However, whether patterns of chronic physical conditions have comparatively different associations with depressive symptoms remains unclear. This study aimed to investigate the associations of physical multimorbidity patterns with depressive symptoms.

**Design** This study was designed as a nationwide cross-sectional survey in Japan.

**Setting** General sample of the Japanese population.

**Participants** Adult Japanese residents were selected by a quota sampling method. Data were analysed from 1788 residents who reported one or more chronic health conditions.

**Results** Among four physical multimorbidity patterns: cardiovascular-renal-metabolic (CRM), skeletal-articular-digestive (SAD), respiratory-dermal (RDE) and malignant-digestive-urolologic (MDU), multivariable logistic regression analyses revealed that the RDE pattern showed the strongest association with depressive symptoms (aOR=1.68, 95% CI: 1.21 to 2.31 for the pattern score highest quartile, compared with the lowest quartile), followed by SAD and MDU patterns (aOR=1.41, 95% CI: 1.01 to 1.98 for the SAD pattern score highest quartile; 1.41, 95% CI: 1.01 to 1.96 for the MDU pattern score highest quartile, compared with the lowest quartile). In contrast, the CRM pattern score was not significantly associated with depressive symptoms (aOR=1.31, 95% CI: 0.90 to 1.89 for the pattern score highest quartile, compared with the lowest quartile).

**Conclusions** Physical multimorbidity patterns have different associations with depressive symptoms. Among these patterns, patients with the RDE pattern may be at a higher risk for developing depressive symptoms. This study reinforces the evidence that cluster pattern of chronic health conditions is a useful measure for clinical management of multimorbidity as it is differently associated with mental health status, which is one of the crucial outcomes for multimorbid patients.

## INTRODUCTION

The number of people suffering from multimorbidity, defined as the simultaneous existence of two or more chronic health conditions within an individual, is currently on the rise, especially in primary care.<sup>1</sup> A

study that was conducted in Japan showed that the prevalence of multimorbidity is 29.9% in adult residents, with the proportion rising to 62.8% in those aged 65 or older.<sup>2</sup>

Depression, one of the leading diseases contributing to global disease burden, needs to be considered if we are to understand the best way to care for patients with multimorbidity.<sup>3</sup> Chronic physical conditions and symptoms are consistently associated with an increased tendency towards depressive symptoms.<sup>4,5</sup> Furthermore, previous studies have shown that depression is two to three times more likely in people with physical multimorbidity compared with people without physical multimorbidity or those who have no chronic physical condition.<sup>6</sup> Although in these studies the associations of the total number of chronic health conditions with depression have been investigated, such an index may be too crude to fully understand how multimorbidity affects depressive symptoms. Non-random cluster patterns of chronic physical conditions may have different associations with depressive symptoms. Indeed, these multimorbidity patterns have been attracting attention from researchers and healthcare providers who aim to understand the complex nature of multimorbidity and improve the quality of care for patients with multimorbidity. Recent studies have used statistical approaches such as factor analysis to identify complex patterns of multimorbidity.<sup>7-10</sup>

Whether physical multimorbidity patterns have different relationships with depressive symptoms has not been investigated before. In the present study, we aim to examine the associations among the different physical multimorbidity patterns with depressive symptoms.

## METHODS

### Design and study population

The data used in this study were collected from the Norm Study, which was conducted in 2016. The Norm Study was a nationwide



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cross-sectional survey that was aimed at collecting data on health-related quality of life, health conditions, healthcare utilisation and sociodemographic characteristics in a general sample of the Japanese population.<sup>2</sup> A quota sampling method was used to select a representative sample of the Japanese general population, aged 16–84, from a resident panel administered by the Nippon Research Center.<sup>11</sup> The resident panel is composed of approximately 300 000 residents in Japan. In this study, quotas were set with regard to age, gender and residential area to make our sample representative of the demographic distribution of Japan, as shown in the most recent census data. Data collection was either web-based for patients aged ≤69 or mail-based for those aged ≥70. In total, 3307 participants responded to the Norm Study, but only adult outpatients aged ≥18 who had one or more chronic health conditions were included in this study.

## Measures

### Chronic health conditions

In total, 17 chronic health conditions were assessed to identify multimorbidity patterns in this study. The following wide range of chronic health conditions was included in the analyses, as these were available in the Norm Study; hypertension, diabetes, dyslipidaemia, stroke, cardiac diseases, chronic respiratory diseases, digestive diseases, kidney diseases, urologic diseases, arthritis or rheumatism, lumbar diseases, neurologic diseases, mental disorders, endocrine diseases, malignancy, vision abnormalities and skin diseases. In a structured questionnaire, participants were asked whether a doctor/nurse/paramedic has ever told you that you have each chronic health condition.

### Depressive symptoms

We used the five-item version of the Mental Health Inventory (MHI-5)<sup>12</sup> to evaluate depressive symptoms. MHI-5 is used as the ‘Mental Health’ domain of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). SF-36 was translated into Japanese,<sup>13</sup> and the Japanese version was validated for use in the general population of Japan.<sup>14</sup> The performance of the Japanese version of MHI-5 in detecting depressive symptoms has been assessed in a previous study.<sup>15</sup> The score for MHI-5 was computed by summing the scores of each question item and then transforming the raw scores to a 100-point scale.<sup>16</sup> According to the previous study, we classified

participants with a score of ≤52 points as having depressive symptoms.<sup>15</sup>

### Covariates

Covariates were selected for their known associations with multimorbidity and depression. We included the following variables as covariates; age, sex, years of education and household income. In the Norm Study, all covariates were assessed using a structured questionnaire.

### Statistical analysis

Descriptive statistics were obtained for the participants’ characteristics. Unadjusted associations between the participants’ characteristics and depressive symptoms were analysed by the  $\chi^2$  test.

Statistical approach was used to identify the non-random cluster patterns of 17 chronic health conditions. Multimorbidity patterns were determined using exploratory factor analysis using multidimensional item response theory. The detailed procedure was reported in our previous study.<sup>2</sup> In this study, we excluded the neuropsychiatric pattern (mental disorders and neurologic diseases) as a non-physical multimorbidity pattern, thus four physical multimorbidity patterns were identified (table 1). Multimorbidity pattern scores for each individual participant were derived using a maximum a posteriori estimation, incorporating both factor loadings and category threshold.<sup>17</sup> The latent means were set to be 0 for each multimorbidity pattern in the Japanese general population. For ease of interpretation, we categorised pattern scores into quartiles.

Multivariable logistic regression analyses were conducted to determine the associations of physical multimorbidity patterns with depressive symptoms. Each of the multimorbidity pattern scores was included individually in the model to avoid multicollinearity. The following individual covariates were included in the analyses: age, sex, years of education and annual household income. All statistical tests were two-sided, and  $p < 0.05$  was considered statistically significant. In all regression analyses, we accounted for missing data on dependent and independent variables by multiple imputation using fully conditional specification. Statistical analyses were performed using R V.3.4.2 (R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org) and psych, mirt and mice packages.

## RESULTS

Out of a total of 3307 study participants, 1788 matched the inclusion criteria, being aged ≥18 and having one or

**Table 1** Identified physical multimorbidity patterns in the Japanese general population

Pattern	Health condition
Cardiovascular-renal-metabolic (CRM) pattern	Hypertension, diabetes, dyslipidaemia, stroke, cardiac diseases and kidney diseases
Skeletal-articular-digestive (SAD) pattern	Arthritis or rheumatism, lumbar diseases and digestive diseases
Respiratory-dermal (RDE) pattern	Chronic respiratory diseases and skin diseases
Malignant-digestive-urologic (MDU) pattern	Malignancy, digestive and urologic diseases

Exploratory factor analysis was used to identify multimorbidity patterns.

**Table 2** Participants' characteristics with or without depressive symptoms: N (%)

Characteristic	Total (n=1788)	Depressive symptoms		P value*
		Present (n=493)	Absent (n=1295)	
<b>Gender</b>				
Male	895 (50.1)	245 (49.7)	650 (50.2)	0.851
Female	893 (49.9)	248 (50.3)	645 (49.8)	
Data missing	0	0	0	
<b>Age (years)</b>				
18–29	156 (8.7)	79 (16.0)	77 (5.9)	<0.001
30–44	290 (16.2)	139 (28.2)	151 (11.7)	
45–64	634 (35.5)	177 (35.9)	457 (35.3)	
65–74	436 (24.4)	52 (10.5)	384 (29.7)	
≥75	272 (15.2)	46 (9.3)	226 (17.5)	
Data missing	0	0	0	
<b>Education level</b>				
Less than high school	81 (4.5)	24 (4.9)	57 (4.4)	0.446
High school	555 (31.0)	142 (28.8)	413 (31.9)	
Junior college	312 (17.4)	99 (20.1)	213 (16.5)	
More than or equal to college	716 (40.1)	212 (43.0)	504 (38.9)	
Data missing	124	16	108	
<b>Annual household income (million JPY)</b>				
<3.00 (≈27 000 US dollar)	493 (27.6)	170 (34.5)	323 (24.9)	0.097
3.00–4.99	527 (29.5)	114 (23.1)	413 (31.9)	
5.00–6.99	321 (18.0)	91 (18.5)	230 (17.8)	
7.00–9.99	241 (13.5)	71 (14.4)	170 (13.1)	
≥10.00	168 (9.4)	41 (8.4)	127 (9.8)	
Data missing	38	6	32	
<b>Number of morbidities</b>				
1	815 (45.6)	234 (47.5)	581 (44.9)	0.461
2	445 (24.9)	116 (23.5)	329 (25.4)	
≥3	528 (29.5)	143 (29.0)	385 (29.7)	
Data missing	0	0	0	

\*P value by  $\chi^2$  test for trend.

more chronic health conditions. **Table 2** shows the characteristics of the study population. The proportion of elderly participants aged  $\geq 65$  was 39.6%. Multimorbidity was found in 973 participants (54.4%), and depressive symptoms, defined as an MHI-5 score of  $\leq 52$  points, were found in 493 participants (27.6%). **Table 2** also compares the characteristics of the participants who had depressive symptoms against those who did not have any. Trends in the data suggested that the participants with depressive symptoms were younger.

**Table 3** shows the unadjusted association between each chronic health condition and depressive symptoms. Hypertension, dyslipidaemia, vision abnormalities, skin diseases and mental disorders were significantly associated with depressive symptoms.

**Figure 1** shows the adjusted associations between physical multimorbidity pattern scores and depressive symptoms.

The RDE pattern score had the strongest association with depressive symptoms (adjusted odds ratio (aOR)=1.68, 95% CI: 1.21 to 2.31 for the pattern score highest quartile, compared with the lowest quartile). SAD and MDU pattern scores were also significantly associated with depressive symptoms (aOR=1.41, 95% CI: 1.01 to 1.98 for the SAD pattern score highest quartile; 1.41, 95% CI: 1.01 to 1.96 for the MDU pattern score highest quartile, compared with the lowest quartile). In contrast, the CRM pattern score was not significantly associated with depressive symptoms (aOR=1.31, 95% CI: 0.90 to 1.89 for the pattern score highest quartile, compared with the lowest quartile).

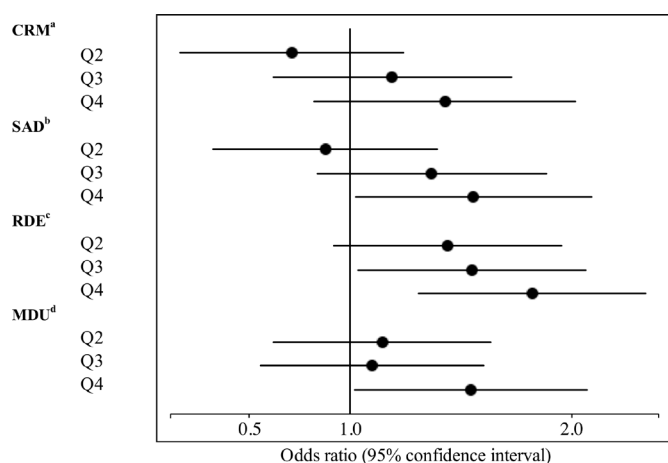
## DISCUSSION

In a representative sample of Japanese adults with chronic health conditions, we found that physical multimorbidity

**Table 3** Prevalence of chronic health conditions by depressive symptoms: %

Chronic health condition	Depressive symptoms		P value*
	Present (n=493)	Absent (n=1295)	
Hypertension	28.4	38.7	<0.001
Lumbar diseases	21.7	23.0	0.555
Dyslipidaemia	16.2	20.5	0.043
Digestive diseases	19.3	16.8	0.226
Vision abnormalities	11.6	19.5	<0.001
Skin diseases	21.3	13.8	<0.001
Mental disorders	25.2	8.2	<0.001
Chronic respiratory diseases	13.2	10.4	0.098
Arthritis or rheumatism	9.5	11.8	0.171
Diabetes	9.1	11.6	0.137
Urologic diseases	7.7	10.3	0.091
Malignancy	7.7	7.1	0.660
Cardiac diseases	6.7	7.0	0.804
Kidney diseases	4.3	4.3	0.952
Endocrine diseases	3.4	4.4	0.366
Stroke	3.4	3.2	0.828
Neurologic diseases	2.0	1.5	0.401

\*P value by  $\chi^2$  test.



**Figure 1** Associations of physical multimorbidity pattern scores with depressive symptoms (n=1788): adjusted for age, sex, education level and annual household income. Each pattern score was included individually in the model; Reference, Q1. <sup>a</sup>Cardiovascular-renal-metabolic (CRM) pattern score quartiles: Q1, -0.30 to 0.10; Q2, 0.10 to 0.60; Q3, 0.60 to 1.14; Q4, 1.14 to 3.09. <sup>b</sup>Skeletal-articular-digestive (SAD) pattern score quartiles: Q1, -0.18 to 0.19; Q2, 0.20 to 0.45; Q3, 0.46 to 1.04; Q4, 1.04 to 2.82. <sup>c</sup>Respiratory-dermal (RDE) pattern score quartiles: Q1, -0.22 to 0.12; Q2, 0.13 to 0.43; Q3, 0.43 to 0.77; Q4, 0.77 to 2.81. <sup>d</sup>Malignant-digestive-urologic (MDU) pattern score quartiles: Q1, -0.07 to 0.10; Q2, 0.10 to 0.37; Q3, 0.37 to 0.70; Q4, 0.70 to 3.41.

patterns have different associations with depressive symptoms. The RDE pattern had the strongest association with depressive symptoms, followed by the SAD and MDU

patterns. Our findings reinforced the significance of understanding multimorbidity patterns when assessing depressive symptoms in patients with chronic physical conditions.

A high prevalence of depression has been reported among patients with various chronic physical conditions, such as diabetes, stroke, chronic respiratory diseases, digestive diseases, rheumatism, lumbar diseases, malignancy and skin diseases.<sup>18–25</sup> In addition, previous studies have associated the total number of chronic physical conditions with depression.<sup>6</sup> However, until now, it remains unclear which multimorbidity patterns are strongly associated with it. This study adds to current knowledge by considering the categorical effect of physical multimorbidity patterns on depressive symptoms rather than the cumulative one.

Several hypotheses about the mechanisms of how specific physical multimorbidity patterns influence depressive symptoms exist. For example, in our previous study, we demonstrated that RDE, SAD and MDU patients have a higher dosage frequency, which can induce a treatment burden,<sup>2</sup> which is defined as the ‘work’ of being a patient and its effect on the patient’s quality of life.<sup>26</sup> As such, the higher dosage frequency and multiple dosage forms (oral medicines, inhalants and topical medicines), common in patients with the RDE (eg, asthma and atopic dermatitis), may increase the risk for depressive symptoms through increased treatment burden. Alternatively, a twin study reported that patients with asthma and those with atopic dermatitis are genetically vulnerable to depressive disorders.<sup>27</sup> It is possible for the RDE pattern and depressive symptoms to share a genetic risk. However, future studies are

warranted to determine, more precisely, how physical multimorbidity patterns affect depressive symptoms.

This is the first study comparing the associations of different physical multimorbidity patterns with depressive symptoms. Our findings are strengthened by some aspects of the study design. The study results were based on data from a nationwide representative sample of the Japanese general adult population. Using this data allows for the generalisation of the results. Furthermore, the applied physical multimorbidity patterns in the Japanese general population were generated using an advanced method of multidimensional item response theory.<sup>2</sup>

However, the study had some potential limitations. First, the data were cross-sectional, and causal associations between multimorbidity patterns and depressive symptoms cannot be definitely established. Second, the quota sampling method does not provide all population characteristics an equal or known probability for being selected but ensures that the sample is representative of the quota-defining characteristics. Therefore, some selection bias may have affected our results. Third, although self-reported data are commonly used to identify multimorbidity patterns in the general population,<sup>7–10</sup> this method of assessment may have introduced misclassification bias and selection bias. Indeed, participants did not include patients with diseases, such as advanced dementia. Fourth, although the performance of MHI-5 in detecting depressive symptoms has been established, assessment using this tool does not fulfil the criteria of a definitive diagnosis of depression.

## CONCLUSION

Our study showed that physical multimorbidity patterns have different associations with depressive symptoms. Among these patterns, patients with the RDE pattern may be at a higher risk for developing depressive symptoms. This study reinforces the evidence that cluster pattern of chronic health conditions is a useful measure for clinical management of multimorbidity as it is differently associated with mental health status, which is one of the crucial outcomes for multimorbid patients.

### Key points

- ▶ Do physical multimorbidity patterns have different relationships with depressive symptoms? Which pattern does have the strongest association with depressive symptoms?
- ▶ Physical multimorbidity patterns have different associations with depressive symptoms. The respiratory-dermal pattern had the strongest association with depressive symptoms, followed by the skeletal-articular-digestive and malignant-digestive-urolologic patterns.
- ▶ In patients with chronic health conditions, the assessment of depression should include multimorbidity recognised as patterns, considered beyond the total number of health conditions.

**Acknowledgements** We thank the staff members of the Manami Imai (Nippon Research Centre) for their assistance with the administration of this study.

**Contributors** All authors (TA, YY, SS and SF) of the paper contributed to the conception or design of the work. TA performed the statistical analyses. TA and YY interpreted the analyses. TA drafted the manuscript. All authors reviewed and edited the manuscript, contributed to the discussion of the data and performed critical review of the manuscript. All authors gave the final approval of the manuscript before submission.

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The institutional review board of the Institute for Health Outcomes and Process Evaluation Research (iHope International) provided the ethical approval for this study (approval no 201611).

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request.

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