

# Bidirectional Association Between Probable Depression and Multimorbidity Among Middle-Aged and Older Adults in Thailand

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**Introduction:** The purpose of this study was to assess the bidirectional association between multimorbidity (MM) and probable depression in a longitudinal study in Thailand.

**Methods:** We analyzed longitudinal data of participants 45 years and older from two consecutive waves (in 2015 and 2017) of Health, Aging, and Retirement in Thailand (HART). Probable depression was assessed using the Center for Epidemiological Studies Depression scale. Logistic regression analysis was conducted to assess the association between baseline probable depression and incident physical MM, and baseline physical MM and incident probable depression.

**Results:** In all, 2712 participants without MM at baseline and 2684 without probable depression at baseline were included. At follow-up 15.6% of probable depression cases and 11.4% of nonprobable depression cases developed physical MM, and at follow-up 13.3% of physical MM cases and 8.9% of nonphysical MM cases developed probable depression. In the final logistic regression analysis, adjusted for age, sex, marital status, income, education, body mass index, physical activity, smoking tobacco, alcohol use, and social engagement, probable depression at baseline was positively associated with incident physical MM (aOR: 1.50, 95% CI: 1.09 to 2.06), and physical MM at baseline was positively associated with incident probable depression (aOR: 1.47, 95% CI: 1.07 to 2.02).

**Discussion:** Baseline physical MM increases the risk of incident probable depression and baseline probable depression increases the risk of incident physical MM among middle-aged and older adults in Thailand.

**Keywords:** multimorbidity, depression, longitudinal study, Thailand

## Introduction

Thailand has been undergoing a epidemiological and demographic transition, increasing ageing and chronic non-communicable diseases.<sup>1,2</sup> This may include multimorbidity (MM) (co-existence of  $\geq 2$  chronic conditions) and depression increasing the burden on the health-care systems.<sup>3,4</sup> Compared to people without MM, people with MM are two to three times more likely to have depression.<sup>5</sup> MM can have various negative health outcomes, such as disability, mental morbidity, higher health-care utilisation, and mortality.<sup>5,6</sup> Depression in later life may increase comorbidity, reduce quality of life, social functioning,<sup>7</sup> suicidal behaviour,<sup>8</sup> and mortality.<sup>9</sup>

In low- and middle-income countries (LMICs) the prevalence of MM was 29.7%,<sup>10</sup> in Thailand 30.4% among the general adult population,<sup>11</sup> among ageing adults in six LMICs, the prevalence of physical MM was 45.5%,<sup>12</sup> and among older adults in southern Thailand, the prevalence of MM was 16.8%.<sup>13</sup> Among older adults, the global prevalence of depression was 28.4%,<sup>14</sup> 15.2% in India,<sup>15</sup> 11.5% in Malaysia,<sup>16</sup> and in local studies in Thailand, the prevalence of probable depression ranged from 18.5%<sup>17</sup> to 28.5%.<sup>18</sup>

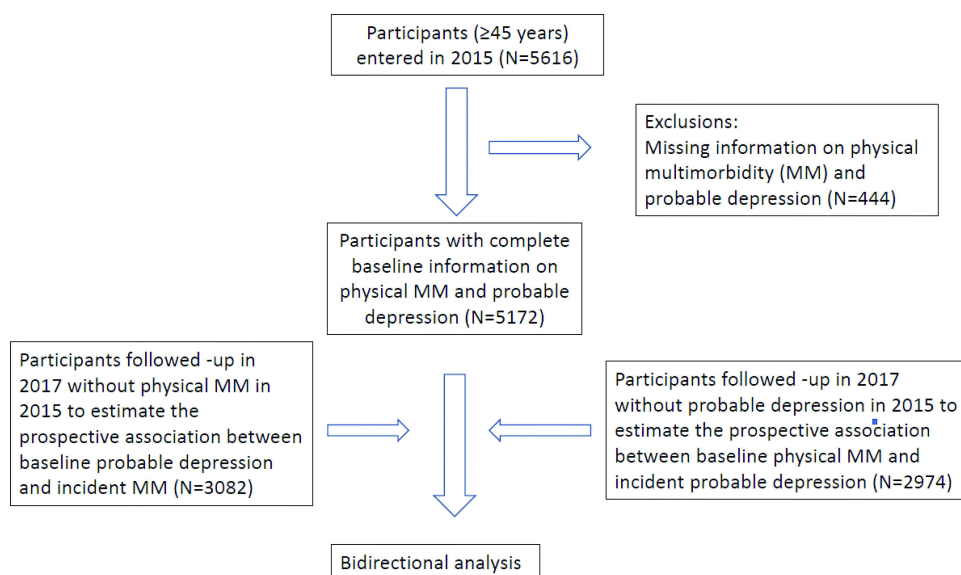
Depression and MM are complex multifactorial conditions, and in unidirectional longitudinal studies, most investigations show an association between MM and incident depression, while fewer studies found an association between depression and incident MM, suggesting a possible bidirectional association between MM and depression.<sup>19</sup> So far, it appears that only two studies, namely from the China Health and Retirement Study, showed a bidirectional association between probable depression and MM<sup>20</sup> and self-reported diagnosed “hypertension, dyslipidaemia, diabetes, cancer, chronic lung disease, liver disease, heart problems, stroke, kidney disease, stomach or other digestive diseases, memory-related disease, arthritis or rheumatism and asthma”.<sup>21</sup> More studies are needed to investigate the bidirectional associations MM and depression to gain a better understanding of this relationship that can help improve the prevention and treatment of MM and depression.<sup>19</sup> Consequently, the objective of this study was to investigate the bidirectional association between probable depression and MM among middle-aged and older adults in Thailand.

## Methods

### Participants

We analyzed longitudinal data from two consecutive waves (2015 and 2017) of the Health, Aging, and Retirement in Thailand (HART) cohort study. From the total population and household data in Thailand, a three-stage (regions, province, blocks, or villages) stratified random sampling was employed. In each household, one person ( $\geq 45$  years) was randomly selected, being the inclusion criterium. Proxy interviews were conducted for frail participants.<sup>22</sup> The 2015 survey (from February to July) (N=5616) and 2017 survey (from January to June 2017) included 3,708 members of the 2015 HART cohort (192 died over the follow-up or 4.3% of the baseline respondents who were in the study area; 1,554 moved away from the study area; 270 declined participation; and the response rate: 72.33% and the retention rate: 66.03%).<sup>22</sup> A total of 3708 participants who responded to 2015 and 2017 survey were included in the study, and 3407 had complete information on our variables of interest (physical MM, and probable depression) (see Figure 1).

Participants were interviewed at their homes by trained field workers after written informed consent was obtained. The study was approved by the “Ethics Committee in Human Research, National Institute of Development Administration – ECNIDA (ECNIDA 2020/00012).” The study complies with the Declaration of Helsinki.



**Figure 1** Study flow chart.

## Measures

### Outcome Variables

Chronic physical conditions were evaluated by self-reported health-care provider diagnosed conditions, including hypertension, diabetes, lung disease, emphysema, cardiovascular disease, heart disease, heart failure, rheumatism, arthritis, bone disease, low bone density, osteoporosis, kidney disease, cancer, and liver disease. Multimorbidity (MM) was defined as having two or more physical chronic conditions, and no MM as having no or one physical chronic condition.

Probable depression ( $\geq 10$  scores) was defined using the Depression Scale of the Center for Epidemiologic Studies (CES-D-10).<sup>23</sup> The CES-D-10 had a reliability coefficient of 0.78 in wave 1 and 0.72 in wave 2 in this study. Previous studies have shown adequate validity of the CES-D-10 in the Thai (older) adult population.<sup>24,25</sup>

#### Independent variables

Social and demographic indicators: educational level, sex, age, marital status, and annual income quartile “1=0 to <380 US\$, 2=380 to <1642, 3=1642 to <4093, 4 $\geq$ 4093 US\$”.

Tobacco use: “Have you ever smoked cigarettes?” (response options: “1=yes, and still smoke now, 2=yes, but quit smoking, and 3=never”).

Alcohol use: “Have you ever drunk alcoholic beverages such as liquor, beer, or wine?” (response options: “1=yes, and still drinking now, 2=yes, but do not drink now, and 3=never”).

Physical activity in the past week was divided into “none=inactivity, 1–149 min/week=low activity, and  $\geq 150$  min/week=high activity.”<sup>26,27</sup>

Body Mass Index (BMI): self-reported body weight and height, classified into “underweight ( $<18.5$  kg/m<sup>2</sup>), normal weight (18.5–22.9 kg/m<sup>2</sup>), overweight (23–24.9 kg/m<sup>2</sup>), and obesity (25+ kg/m<sup>2</sup>).”<sup>28</sup>

Social engagement included six items of formal social engagement (eg, participation in religious organisations) and one item of informal social engagement (meeting with close friends or relatives) and was defined as at least one activity in the past month.<sup>22,29</sup>

## Data Analysis

Proportions of older adults with incident MM and incident probable depression are presented with frequencies and percent. Pearson chi-square tests are used to compare baseline characteristics among groups. The first logistic regression model estimated odds ratios (OR) and confidence intervals (CI) for baseline probable depression and incident MM, and the second model compared baseline MM and incident probable depression. Three models are presented for incident MM and incident probable depression. The first model is unadjusted, in the second model adjustments are made for age, income, sex, education, and marital status, and in the third model adjustments are made for model 2 variables plus smoking, physical activity, body mass index, alcohol use, and social engagement.  $p \leq 0.05$  was considered statistically significant. Missing values were excluded from the analyses. All statistical analyses were done with StataSE 15.0 (College Station, TX, USA).

## Results

### Sample Characteristics

In the first model that estimates incident physical MM, a total of 2712 nonphysical MM individuals were included from baseline, with 320 (11.3%) having probable depression at baseline. At follow-up 15.6% of the probable depression cases and 11.4% of non-probable depression cases developed physical MM. Middle-aged and older adults with probable depression at baseline have a significantly higher prevalence of physical MM at follow-up ( $p < 0.001$ ). Those with physical MM were more likely to be older, not married, had a lower income, had a higher body mass index, had no social engagement, and had never smoked tobacco than those without physical MM (see Table 1)

In the second model that estimates incident probable depression, a total of 2684 individuals with non-probable depression were included from baseline, with 484 (16.2%) having MM at baseline. At follow-up 13.3% of MM cases and 8.9% of non-MM cases developed probable depression. Middle-aged and older adults with a physical MM at baseline

**Table I** Sample Characteristics of Participants with Incident Physical Multimorbidity, Thailand, 2015–2017

Variables	Subcategories	Incident Physical Multimorbidity		p-value
		No (n=2712)	Yes (n=370)	
		N (%)	N (%)	
Age (in years)	45–54	597 (94.3)	36 (5.7)	<0.001
	55–64	777 (90.3)	83 (9.7)	
	66–74	636 (83.7)	124 (16.3)	
	75 or more	702 (84.7)	127 (15.3)	
Sex	Female	1407 (88.0)	192 (12.0)	0.997
	Male	1305 (88.0)	178 (12.0)	
Education	None	159 (84.1)	30 (15.9)	0.096
	Elementary	2079 (87.9)	286 (12.1)	
	>Elementary	468 (90.0)	52 (10.0)	
Marital status	Not married	1042 (86.5)	163 (13.5)	0.038
	Married/cohabiting	1668 (89.0)	207 (11.0)	
Income quartile	Low	623 (86.8)	95 (13.2)	<0.001
	Lower middle	629 (85.0)	111 (15.0)	
	Upper middle	713 (87.7)	100 (12.3)	
	High	747 (92.1)	64 (7.9)	
Alcohol use	Never	2163 (87.5)	310 (12.5)	0.061
	Past	180 (87.4)	26 (12.6)	
	Current	369 (91.6)	34 (8.4)	
Smoking tobacco use	Never	2125 (87.0)	318 (13.0)	<0.001
	Past	206 (89.2)	25 (10.8)	
	Current	381 (93.4)	27 (6.6)	
Physical activity	None	1568 (87.5)	223 (12.5)	0.078
	1–149 min./week	682 (87.1)	101 (12.9)	
	≥150 minutes/week	462 (90.9)	46 (9.1)	
Body mass index	Normal	977 (90.1)	107 (9.9)	<0.001
	Under	277 (89.1)	34 (10.9)	
	Overweight	490 (88.3)	65 (11.7)	
	Obesity	682 (83.8)	132 (16.2)	
Social engagement	No	162 (83.5)	32 (16.5)	0.048
	Yes	2545 (88.3)	338 (11.7)	

(Continued)

**Table 1** (Continued).

Variables	Subcategories	Incident Physical Multimorbidity		p-value
		No (n=2712)	Yes (n=370)	
		N (%)	N (%)	
Probable depression	No	2370 (88.5)	307 (11.4)	0.018
	Yes	342 (88.4)	63 (15.6)	

have a significantly higher prevalence of probable depression at follow-up ( $p < 0.001$ ). Those with probable depression were more likely to be older, not married, and had lower income than those without probable depression (see [Table 2](#)).

## Odds Ratios for Bidirectional Associations Between Probable Depression and Physical Multimorbidity

In the final logistic regression model, adjusted for education, income, age, marital status, sex, smoking tobacco, body mass index, alcohol use, physical activity, and social engagement, probable depression at baseline was positively associated with incident physical MM (aOR: 1.50, 95% CI: 1.09 to 2.06), and physical MM at baseline was positively associated with incident probable depression (aOR: 1.47, 95% CI: 1.07 to 2.02) (see [Table 3](#)).

**Table 2** Sample Characteristics of Participants with Incident Probable Depression, Thailand, 2015–2017

Variables	Subcategories	Incident Probable Depression		p-value
		No (n=2684)	Yes (n=290)	
		N (%)	N (%)	
Age (in years)	45–54	518 (91.0)	51 (9.0)	0.036
	55–64	747 (92.5)	61 (7.5)	
	66–74	684 (89.2)	83 (10.8)	
	75 or more	735 (88.6)	95 (11.4)	
Sex	Female	1399 (89.5)	164 (10.5)	0.151
	Male	1285 (91.1)	126 (8.9)	
Education	None	143 (89.9)	16 (10.1)	0.084
	Elementary	2073 (89.7)	237 (10.3)	
	>Elementary	464 (93.0)	35 (7.0)	
Marital status	Not married	1065 (88.2)	143 (11.8)	0.002
	Married/cohabiting	1619 (91.7)	147 (8.3)	
Income quartile	Low	576 (88.6)	74 (11.4)	<0.001
	Lower middle	666 (88.0)	91 (12.0)	
	Upper middle	733 (90.6)	76 (9.4)	
	High	709 (93.5)	49 (6.5)	

(Continued)

**Table 2** (Continued).

Variables	Subcategories	Incident Probable Depression		p-value
		No (n=2684)	Yes (n=290)	
		N (%)	N (%)	
Alcohol use	Never	2156 (90.1)	237 (9.9)	0.455
	Past	187 (89.0)	23 (11.0)	
	Current	341 (91.9)	30 (8.1)	
Smoking tobacco use	Never	3148 (90.2)	234 (9.8)	0.867
	Past	203 (89.8)	23 (10.2)	
	Current	333 (91.0)	33 (9.0)	
Physical activity	None	1496 (89.6)	174 (10.4)	0.376
	1–149 min./week	718 (91.0)	71 (9.0)	
	≥150 minutes/week	470 (91.3)	45 (8.7)	
Body mass index	Normal	895 (88.8)	113 (11.2)	0.273
	Under	245 (90.4)	26 (9.6)	
	Overweight	513 (91.8)	46 (8.2)	
	Obesity	783 (90.5)	82 (9.5)	
Social engagement	No	184 (91.1)	18 (8.9)	0.677
	Yes	2500 (90.2)	272 (9.8)	
Physical multimorbidity	No	2180 (91.1)	212 (8.9)	<0.001
	Yes	501 (86.7)	77 (13.3)	

**Table 3** Odds Ratios for Bidirectional Associations Between Probable Depression and Physical Multimorbidity (MM)

Variable	Sub-Category	Model 1 (N=3082) (R <sup>2</sup> =0.003)		Model 2 (N=3074) (R <sup>2</sup> =0.03)		Model 3 (N=2746) (R <sup>2</sup> =0.06)	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
		Odds ratios for the association between probable depression at baseline and incident physical MM					
Probable depression	No	1 (Reference)		1 (Reference)		1 (Reference)	
	Yes	1.44 (1.04 to 1.99)	0.028	1.37 (1.02 to 1.82)	0.033	1.50 (1.09 to 2.06)	0.013
		<b>Model 1 (N=2974) (R<sup>2</sup>=0.007)</b>		<b>Model 2 (N=2968) (R<sup>2</sup>=0.02)</b>		<b>Model 3 (N=2697) (R<sup>2</sup>=0.02)</b>	
		<b>OR (95% CI)</b>	<b>p-value</b>	<b>OR (95% CI)</b>	<b>p-value</b>	<b>OR (95% CI)</b>	<b>p-value</b>
		Odds ratios for the association between physical MM at baseline and incident probable depression					
Physical MM	No	1 (Reference)		1 (Reference)		1 (Reference)	
	Yes	1.64 (1.23 to 2.20)	<0.001	1.57 (1.12 to 2.03)	0.007	1.47 (1.07 to 2.02)	0.019

**Notes:** Model 1: unadjusted; Model 2: adjusted for age, sex, marital status, education, and income; Model 3: adjusted for Model 2 variables plus body mass index, physical activity, smoking, alcohol use, and social engagement.

## Discussion

This is the first longitudinal study investigating the bidirectional associations between MM and probable depression in Southeast Asia. Consistent with two studies in China,<sup>20,21</sup> we found that physical MM (hypertension, diabetes, lung disease, emphysema, cardiovascular disease, heart disease, heart failure, rheumatism, arthritis, bone disease, low bone density, osteoporosis, kidney disease, cancer, and liver disease) and probable depression were bidirectionally associated among older adults in Thailand. These associations were independent of body mass index, sex, marital status, age, education, income, smoking, physical activity, alcohol use, and social engagement.

Other previous studies have shown a bidirectional association between depression or depressive symptoms and specific chronic conditions, such as chronic kidney disease,<sup>30</sup> rheumatoid arthritis,<sup>31</sup> chronic lung disease,<sup>32</sup> type 2 diabetes,<sup>33</sup> ischaemic heart disease, and stroke,<sup>34</sup> and hypertension.<sup>35</sup> Therefore, the bidirectional association between physical MM and probable depression can be attributed in part to the specific chronic disease that has a stronger effect on probable depression among those with physical MM. For example, we found that diabetes and rheumatism or arthritis had a higher prevalence of incident probable depression (see [Appendix 1](#)).

Possible mechanisms that could explain the bidirectional association between MM and probable depression may include 1) shared risk factors, such as older age, obesity, physical inactivity, smoking, and alcohol use, for both MM and probable depression,<sup>20</sup> 2) the immune-inflammatory effects stemming from specific chronic conditions, such as heart disease, arthritis, and hypertension, may influence the development of probable depression,<sup>19</sup> 3) having MM may negatively impact various body organs increasing disempowerment and negative emotions leading to probable depression,<sup>36</sup> and 4) the effects of peripheral immune dysfunction among people with probable depression on specific chronic conditions, such as arthritis and hypertension.<sup>20,37</sup>

Clinical implications may include screening and treatment of depression in patients with MM as well as screening and treatment of MM in patients with depression.<sup>5,38</sup> This cohort study only had a 2-year follow-up period, and future studies should be conducted over a longer time frame to assess more comprehensively multiple interacting pathways.<sup>19</sup>

## Study Strength and Limitations

The study utilized a national cohort study with a large sample size, and we adjusted for various confounding social, health, and demographic factors. Study limitations include that MM was assessed by self-reported diagnosed chronic conditions, depression was only measured with a screening questionnaire, and no objective measurements were used. Furthermore, MM could change over time, causing classification bias.

## Conclusion

Baseline physical MM increases the risk of incident probable depression and baseline probable depression increases the risk of incident physical MM among middle-aged and older adults in Thailand. Results may help guide the prevention and treatment of MM and probable depression concurrently in middle and late adulthood in Thailand.

## Acknowledgment

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## Disclosure

The authors report no conflicts of interest in this work.

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