

# Personal, behavioral, and perceived environmental factors associated with late-life depression in older men and women

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**Introduction:** Previous investigations on factors associated with depression were highly focused on personal characteristics and health behaviors; however, few studies used an ecological perspective on the issue, much less on sex differences. This study examined the factors associated with depression, including any sex differences.

**Methods:** A total of 1025 Taiwanese adults older than 65 years were recruited. Their personal demographics, lifestyle behaviors, and perceived environmental factors were obtained through a telephone-based survey. The multiple factors associated with depression in older adults were examined using logistic regression analyses.

**Results:** Fully logistic regression analyses revealed that poor self-rated health (odds ratio =2.54) was correlated with a greater likelihood of depression. Aside from poor self-rated health, being older, sufficient leisure time spent in walking, and perceptions of a safe environment were associated with lower risks of depression in older men, whereas having hypertension and excessive TV viewing were associated with higher risks of depression in older women.

**Conclusion:** Apart from self-rated health, sex differences in the associations of factors such as leisure-time walking, TV watching, and safe traffic environment with depression were observed among older adults. Strategies applied for geriatric depression prevention should take into consideration different sex group.

**Keywords:** geriatric depression, older adults, multiple factors

## Background

Depression is a major cause of life impairment worldwide. Its symptoms may cause negative consequences such as disability and suicide;<sup>1</sup> it also results in economic burden, including the costs related to mental health services and the loss of productivity derived from depression.<sup>2</sup> A meta-analysis, mostly from the United States and Europe, showed a pooled prevalence of depressive disorders was 17.1% among community-based older adults aged 75 years and above.<sup>3</sup> A longitudinal study using national representative population for older adults aged 65 and above showed the incidence rate of depression was 19.7% across four years (2000–2003) in Taiwan.<sup>4</sup> There was evidence showing that there were sex differences in depression. For example, a study comprised 23 European countries found female adults reported higher level of depression than male adults.<sup>5</sup> Another study from Taiwan also reported that the prevalence of depression among older adults was higher in women (12.4%) than in men (7.8%).<sup>6</sup> While considering older adults aged 65 and

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above account for 14.6% of a total population in Taiwan,<sup>7</sup> there is an urgent need to identify the multiple factors associated with depression among the older population in order to develop effective prevention strategies.

An effective strategy of improving early detection is to investigate older adults' characteristics and identify the at-risk population. Previous research has indicated some personal characteristics (eg, sex and health status)<sup>8,9</sup> and behavioral factors (eg, the level of physical activity)<sup>10</sup> were associated with risk of depressive symptoms. However, macro-level depression prevention should also consider other modifiable lifestyle factors such as environmental attributes according to ecological perspectives<sup>11</sup> but few studies have investigated on the environmental factors. Identifying the associations of environmental factors with depression is critical for developing future interventions. Older adults tend to spend most of their time near their neighborhood due to their declined mobility.<sup>12</sup> Therefore, if the neighborhood environment is not safe, it may cause sources of chronic stressor and fears.<sup>13</sup> Limited evidence showed that poor environmental safety is associated with higher odds of depression in older adults,<sup>14,15</sup> however, whether there were sex differences still need further investigation. This study examined the associations of multiple levels of factors, including personal, behavioral, and environmental factors, with depression among older adults, with a particular focus on sex differences.

## Materials and methods

### Participants

The participants in the present study were recruited for a cross-sectional population-based survey, which was conducted in November 2016 in Taiwan through a computer-assisted telephone interviewing system. In that year, Taiwan was estimated to have a population of 23,539,816 and a total of 13.2% were the target population aged 65 years and above (N=3,106,105).<sup>16</sup> The required sample size for the present study was calculated to be 1025 older adults with a 95% confidence level and a 3% confidence interval. These participants were randomly sampled by their residual areas in the beginning, and then by their sex and age group. All the interviewers had experience in administering telephone surveys and had been trained in using a standardized form to ask questions before the survey started. Participants were not offered any rewards for participating, and verbal informed consent was obtained before the start of each telephone interview. The

study protocols were reviewed and approved by the Ethics Committee of National Taiwan Normal University (201605HM006).

### Outcome variable

Geriatric Depression Scale-4 (GDS-4) is a short-form depression scale which has an acceptable level of internal consistency (Cronbach's alpha=0.55).<sup>17</sup> The questionnaire was suggested to be used in screening depression in older adults<sup>17</sup> and was used in telephone survey.<sup>18</sup> In the present study, depression was measured using the Chinese version of the GDS-4. The questionnaire was examined as a high sensitivity and specificity (area under the curve=0.76) instrument and could be used to assess depression in older Taiwanese adults.<sup>19</sup> Participants were required to state their mental status over the past week in terms of the following questions from the four-item version: (1) "Are you basically satisfied with your life?"; (2) "Do you feel that your life is empty?"; (3) "Are you afraid that something bad is going to happen to you?"; and (4) "Do you feel happy most of the time?" Each question was dichotomized into "yes" or "no." The total score for the GDS-4 ranges from 0 to 4 (answering "yes" to questions 1 and 4 and "no" to questions 2 and 3 counted as 1 point each). When different cutoff points were compared, the sensitivity and specificity for the GDS-4 were, respectively, 89% and 65% (cutoff point 0/1) and 61% and 81% (cutoff point 1/2).<sup>17</sup> In the present study, we defined older adults with depression as a score of more than 0 point due to the improved sensitivity and specificity.

### Personal factors

#### Sociodemographic variables

The sociodemographic variables covered in the present study were sex, age (continuous), residential area, education, occupation, marital status, accommodation status, and body mass index (BMI; dividing self-reported weight by the square of height). Residential area was classified into "metropolitan" and "nonmetropolitan." Educational status was categorized into "high school degree or lower" and "university degree or higher." Occupational type was divided into "not full-time job" and "full-time job," and marital status was divided into "married" and "unmarried" (including widowed and divorced). Accommodation status was categorized into "living with others" and "living alone." BMI was divided into "non-overweight (<24 kg/m<sup>2</sup>)" and "overweight (≥24 kg/m<sup>2</sup>)" according to the definitions provided by the Health Promotion

Administration, Ministry of Health and Welfare of Taiwan.<sup>20</sup>

### Diseases and self-rated health status

The most common chronic diseases among older adults in Taiwan are hypertension, diabetes mellitus, and cardiovascular disease. Therefore, participants were asked according to the following questions: "Have you ever been diagnosed by a doctor as having the following diseases, or are you currently taking medication for them?" Each question (regarding hypertension, diabetes mellitus, and cardiovascular disease) was divided into three options: "yes," "no," and "unknown." A choice of "unknown" was categorized as missing data. An additional question regarding self-rated health status was also included, with answers divided into "good" and "poor."

## Behavioral factors

### Leisure time walking and TV viewing

Leisure time spent in walking was acquired using the Taiwanese version of the International Physical Activity Questionnaire (IPAQ), long version. The IPAQ is suitable for and widely used in telephone-based surveys among middle-aged-to-older adults.<sup>21,22</sup> The test-retest reliability of the IPAQ in the present study was 0.78 and the criterion validity compared with accelerometers was 0.31–0.41.<sup>23</sup> Leisure time spent in walking was calculated by multiplying the frequency (d/wk) by the duration of leisure time (mins/d), according to the Kolmogorov-Smirnov test, and the resulting distribution was skewed. On the basis of the Global Recommendations on Physical Activity for Health for older adults,<sup>24,25</sup> this variable was categorized into "sufficient ( $\geq 150$  mins/wk)" and "insufficient ( $< 150$  mins/wk)."

Time spent in watching TV or videos was obtained from the Measure of Older Adults' Sedentary Time questionnaire. The item has an acceptable level of test-retest reliability (intraclass correlation coefficient=0.69; Spearman  $\rho=0.67$ ) in the version translated into Chinese, and can be used to investigate sedentary behavior among Taiwanese older adults.<sup>21,26</sup> The sum of TV viewing time was dichotomized based on 2 hrs/d, which has been reported as a threshold for health risks.<sup>27,28</sup> Thus, the variable was divided into "high TV viewing time ( $\geq 2$  hrs/d)" and "low TV viewing time ( $< 2$  hrs/d)."

### Alcohol use, smoking, and diet

Habitual health behaviors such as alcohol use, smoking, and having a balanced diet (three servings of vegetables and two servings of fruits) were also recorded, in

accordance with the literature.<sup>29–31</sup> Each question was dichotomized into "yes" and "no."

## Perceived environmental factors

Perceived neighborhood environmental factors were determined using the Taiwanese version of the International Physical Activity Questionnaire Environmental Module (IPAQ-E). The questionnaire was developed to investigate the relationship between these environmental factors and walking or cycling in diverse countries, including Asian countries.<sup>32</sup> The IPAQ-E questionnaire was used in a previous study on the association between perceptions of the environment and other health behaviors.<sup>33</sup> Two out of the 17 items in the IPAQ-E questionnaire comprised the variables investigated in this study: (1) safety from crime at night and (2) traffic safety, in accordance with the literature.<sup>14,34</sup> Other items that were not empirically associated with depression were excluded. As in previous studies,<sup>22,35</sup> all of the three factors were included using a 4-point Likert scale and transformed into binary items, recorded as "agree" (strongly agree and somewhat agree) and "disagree" (somewhat disagree and strongly disagree).

## Statistical analysis

The data of 1025 older Taiwanese adults who completed the questionnaire for the present study were analyzed. Chi-squared tests were used to evaluate the proportional differences in variables by sex, and logistic regression models were used to analyze the categorical outcome variables and estimate the odds ratios (ORs) of depression. This analysis examined all of the participants as one group first, and then stratified them by sex. Adjusted ORs and 95% confidence intervals (CIs) were calculated for each variable. The data were analyzed in 2016 using SPSS version 23.0 (IBM Corp, Armonk, NY), and the level of significance was set at 0.05.

## Results

### Participant characteristics

A total of 1025 older adults completed this survey, with a response rate of 30.3%. Participants' ages ranged from 65 to 94 years (mean age=72.35 years; standard deviation=6.14). The characteristics of the participants were compared overall and by sex. As shown in Table 1, in this sample, men were older, more likely to live in non-metropolitan areas, have a higher level of education and a full-time job, be married and overweight, be a drinker and

**Table 1** Participant characteristics overall and by sex (n=1025)

Variables	Total	Men	Women	p-value
n (%)	1025	522 (50.9%)	503 (49.1%)	
<b>Personal factors</b>				
<b>Age (year)</b>				0.001*
65–74	677 (66.0%)	319 (61.1%)	358 (71.2%)	
75+	348 (34.0%)	203 (38.9%)	145 (28.8%)	
<b>Residential area</b>				0.003*
Metropolitan	505 (49.3%)	233 (44.6%)	272 (54.1%)	
Non-metropolitan	520 (50.7%)	289 (55.4%)	231 (45.9%)	
<b>Educational status</b>				<0.001**
High school degree and lower	731 (71.3%)	330 (63.2%)	401 (79.7%)	
University and higher	294 (28.7%)	192 (36.8%)	102 (20.3%)	
<b>Occupational type</b>				0.018*
Not full-time	920 (89.8%)	457 (87.5%)	463 (92.0%)	
Full-time	105 (10.2%)	65 (12.5%)	40 (8.0%)	
<b>Marital status</b>				<0.001**
Not married	234 (22.8%)	85 (16.3%)	149 (29.6%)	
Married	791 (77.2%)	437 (83.7%)	354 (70.4%)	
<b>Accommodation status</b>				0.382
Living alone	139 (13.6%)	66 (12.6%)	73 (14.5%)	
Living with others	886 (86.4%)	456 (87.4%)	430 (85.5%)	
<b>BMI</b>				0.022*
Non-overweight	599 (58.4%)	287 (55.0%)	312 (62.0%)	
Overweight	426 (41.6%)	235 (45.0%)	191 (38.0%)	
<b>Hypertension</b>				0.588
Yes	453 (44.2%)	235 (45.0%)	218 (43.3%)	
No	572 (55.8%)	287 (55.0%)	285 (56.7%)	
<b>Diabetes mellitus</b>				0.244
Yes	190 (18.5%)	104 (19.9%)	86 (17.1%)	
No	835 (81.5%)	418 (80.1%)	417 (82.9%)	
<b>Cardiovascular diseases</b>				0.138
Yes	173 (16.9%)	97 (18.6%)	76 (15.1%)	
No	852 (83.1%)	425 (81.4%)	427 (84.9%)	
<b>Self-rated health status</b>				0.138
Good	830 (81.0%)	432 (82.8%)	398 (79.1%)	
Poor	195 (19.0%)	90 (17.2%)	105 (20.9%)	
<b>Depression</b>				0.535
Yes	345 (33.7%)	171 (32.8%)	174 (34.6%)	
No	680 (66.3%)	351 (67.2%)	329 (65.4%)	
<b>Behavioral factors</b>				
<b>Leisure-time walking</b>				0.052
Sufficient	682 (66.5%)	362 (69.3%)	320 (63.6%)	
Insufficient	343 (33.5%)	160 (30.7%)	183 (36.4%)	

(Continued)

**Table 1** (Continued).

Variables	Total	Men	Women	p-value
<b>Television viewing</b>				0.775
Low	508 (49.6%)	261 (50.0%)	247 (49.1%)	
High	517 (50.4%)	261 (50.0%)	256 (50.9%)	
<b>Alcohol use</b>				<0.001**
Yes	113 (11.0%)	98 (18.8%)	15 (3.0%)	
No	912 (89.0%)	424 (81.2%)	488 (97.0%)	
<b>Smoking status</b>				<0.001**
Yes	75 (7.3%)	71 (13.6%)	4 (0.8%)	
No	950 (92.7%)	451 (86.4%)	499 (99.2%)	
<b>Diet behavior</b>				0.427
Yes	819 (79.9%)	412 (78.9%)	407 (80.9%)	
No	206 (20.1%)	110 (21.1%)	96 (19.1%)	
<b>Perceived environmental factors</b>				
<b>Safety from crimes at night</b>				0.036*
Safe	851 (83.0%)	446 (85.4%)	405 (80.5%)	
Not safe	174 (17.0%)	76 (14.6%)	98 (19.5%)	
<b>Traffic safety</b>				0.708
Safe	683 (66.6%)	345 (66.1%)	338 (67.2%)	
Not safe	342 (33.4%)	177 (33.9%)	165 (32.8%)	

Notes: \*P<0.05, \*\*P<0.001.

Abbreviation: BMI, body mass index.

a smoker, and feel safer at night. The prevalence of depression among all the survey participants in this sample was 33.7%, and women (34.6%) had a higher prevalence of depression than men (32.8%).

## Multiple factors associated with depression

Logistic regression analysis was performed on the studied variables for depression. The results yielded four significant overall associations of depression. Older adults who had poor self-rated health (OR=2.54, 95% CI=1.82–3.54) were associated with a higher risk of depression (Table 2).

Table 2 also reveals the significant factors associated with depression by sex. Older men who had poor self-rated health (OR=2.68, 95% CI=1.63–4.41) were more likely to be depressed. By contrast, those who were older (OR=0.96, 95% CI=0.93–0.99), spent more leisure time in walking (OR=0.56, 95% CI=0.36–0.86), and felt safer from traffic (OR=0.61, 95% CI=0.41–0.91) were less likely to be depressed. Furthermore, older women who had hypertension (OR=1.64, 95% CI=1.11–2.45), had poor self-rated health (OR=3.03, 95% CI=1.87–4.91),

and spent excessive time ( $\geq 2$  hrs/d) on watching TV (OR=1.75, 95% CI=1.19–2.58) were more likely to be depressed.

## Discussion

The results reveal that in addition to self-rated health status, differences were observed between older men and women in terms of the personal, behavioral, and perceived environmental factors associated with depression, similar to the findings of a previous study.<sup>10</sup> Being married, sufficient leisure time spent in physical activity, and perceptions of a safe environment were associated with lower risks of depression in older men, whereas excessive TV viewing and having hypertension were associated with higher risks of depression in older women. The findings suggest that sex differences should be considered when developing effective approaches for depression prevention in older adults.

The findings of this study demonstrated that self-rated health was negatively associated with depression, regardless of sex. This supports the findings of previous studies<sup>36,37</sup> and implies that participants' experiences of their own health predict subsequent emotional features. Future interventions

**Table 2** Multiple factors associated with depression by sex

Variables	Total	Men	Women
	OR (95% CI)	OR (95% CI)	OR (95% CI)
<b>Personal factors</b>			
<b>Age (year)</b>	0.98 (0.96–1.00)	0.96 (0.93–0.99)*	1.01 (0.97–1.04)
<b>Residential area</b>			
Metropolitan	0.97 (0.74–1.26)	1.11 (0.76–1.64)	0.88 (0.60–1.28)
Non-metropolitan	1.00	1.00	1.00
<b>Educational status</b>			
High school degree and lower	1.15 (0.85–1.57)	1.16 (0.76–1.75)	1.06 (0.65–1.71)
University and higher	1.00	1.00	1.00
<b>Occupational type</b>			
Not full-time	0.88 (0.57–1.37)	1.20 (0.67–2.16)	0.59 (0.30–1.18)
Full-time	1.00	1.00	1.00
<b>Marital status</b>			
Not married	1.00	1.00	1.00
Married	0.83 (0.58–1.19)	0.56 (0.31–1.02)	1.06 (0.67–1.70)
<b>Accommodation status</b>			
Living alone	1.14 (0.74–1.76)	1.68 (0.86–3.30)	0.72 (0.39–1.33)
Living with others	1.00	1.00	1.00
<b>BMI (kg/m<sup>2</sup>)</b>			
Non-overweight(<24)	1.13 (0.86–1.48)	1.02 (0.69–1.50)	1.31 (0.88–1.95)
Overweight ( $\geq 24$ )	1.00	1.00	1.00
<b>Hypertension</b>			
Yes	1.20 (0.91–1.57)	0.86 (0.58–1.27)	1.64 (1.11–2.45)*
No	1.00	1.00	1.00
<b>Diabetes mellitus</b>			
Yes	1.08 (0.77–1.52)	1.48 (0.92–2.37)	0.65 (0.38–1.10)
No	1.00	1.00	1.00
<b>Cardiovascular diseases</b>			
Yes	0.86 (0.60–1.25)	1.06 (0.64–1.75)	0.63 (0.35–1.13)
No	1.00	1.00	1.00
<b>Self-rated health status</b>			
Good	1.00	1.00	1.00
Poor	2.54 (1.82–3.54)***	2.68 (1.63–4.41)***	3.03 (1.87–4.91)***
<b>Behavioral factors</b>			
<b>Leisure-time walking (mins/week)</b>			
Sufficient ( $\geq 150$ )	0.83 (0.62–1.11)	0.56 (0.36–0.86)**	1.24 (0.81–1.90)
Insufficient (<150)	1.00	1.00	1.00
<b>Television viewing</b>			
Low	1.00	1.00	1.00
High	1.27 (0.97–1.65)	0.94 (0.64–1.37)	1.75 (1.19–2.58)***
<b>Alcohol use</b>			
Yes	1.00	1.00	1.00

(Continued)

**Table 2** (Continued).

Variables	Total	Men	Women
	OR (95% CI)	OR (95% CI)	OR (95% CI)
No	1.34 (0.85–2.11)	1.30 (0.78–2.15)	1.24 (0.39–3.99)
<b>Smoking status</b>			
Yes	1.00	1.00	1.00
No	0.78 (0.46–1.32)	0.87 (0.50–1.53)	0.45 (0.05–3.80)
<b>Diet behavior</b>			
Yes	1.00	1.00	1.00
No	1.01 (0.73–1.40)	0.73 (0.45–1.18)	1.44 (0.91–2.30)
<b>Perceived environmental factors</b>			
<b>Safety from crimes at night</b>			
Safe	0.73 (0.52–1.03)	0.60 (0.35–1.02)	0.71 (0.44–1.16)
Not safe	1.00	1.00	1.00
<b>Traffic safety</b>			
Safe	0.78 (0.59–1.03)	0.61 (0.41–0.91)*	1.01 (0.67–1.51)
Not safe	1.00	1.00	1.00

Notes: \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

Abbreviations: OR, odds ratio; CI, confidence interval.

for depression are suggested to target older adults whose self-rated health status is low.

Apart from self-rated health status, certain other factors were associated with differences in depression between older men and women. Among personal factors, being older was negatively associated with depression in older men, whereas having hypertension was positively associated with depression in older women. Our data showed there was a slightly negative association between age and depression, especially in men. However, previous findings regarding the association between age and depression among older adults were mixed.<sup>10</sup> Further studies using a larger sample size on the association of age and depression are needed. Consistent with our findings, previous studies showed that there was no association of hypertension with geriatric depression,<sup>38</sup> except in women.<sup>6</sup> Compared to men, women tended to spend more time in sitting behavior,<sup>39</sup> which might be one of the causes of hypertension. Future studies are warranted to have a deeper understanding of the association between hypertension and depression by sex. The individual factors involved could be used to identify vulnerable individuals and increase the sensitivity of detection of geriatric depression.

Among behavioral factors, sufficient leisure time spent in walking was associated with a lower risk of depression in older men, whereas excessive TV viewing was associated with a higher risk of depression in older women.

The literature corroborates the findings of previous studies that less leisure time spent in walking is correlated with a higher risk of depression in men<sup>40</sup> and lower total physical activity is correlated with a higher risk of depression in older adults overall.<sup>41</sup> Several explanations have been suggested for interpreting the association between leisure time spent in walking and depression. One is the effect of distraction, namely that participating in physical activity during leisure time may divert negative thoughts and bad mood; another hypothesis is that social contact provides support, which improves mental health.<sup>42</sup> In addition, TV viewing is a specific type of sedentary behavior associated with an increased risk of depression.<sup>43</sup> Some possible explanations could elucidate the association between TV viewing and depression. First, excessive TV viewing may lead to a lack of social interaction,<sup>44</sup> and poor sleep quality,<sup>45</sup> which may result in depression.<sup>46,47</sup> Second, TV viewing can displace or compress the time spent engaging in physical activity, which serves as a protective factor for depression.<sup>44,48</sup> Alternatively, people who had some depressive symptoms were more likely to decrease their active behavior and increase sitting behavior. Future studies on health behavior and depression should consider sex differences.

In the present study, perceptions of safe neighborhood environments, particularly regarding traffic safety, were

also found as associations with a lower risk of depression in older men. The perception of an unsafe environment is a chronic stressor and fears regarding neighborhood safety lead to insufficient social capital (ie, decreased willingness to interact with others)<sup>34</sup> and reduced willingness to engage in outdoor physical activity.<sup>49</sup> Previous studies showed men spent more time on physical activity than women.<sup>39</sup> A perceived lack of environmental safety may indirectly attenuate the negative associations of physical activity with depression and somewhat increase the risk of depression among men. Furthermore, compared to women, men had a higher frequency to use motor vehicles in Taiwan,<sup>50</sup> they may be more sensitive to traffic safety than crime safety. Future longitudinal research examining the associations between different environmental variables and depression by sex is necessary and highly encouraged.

In addition to strategies of behavioral change, the present study further highlights that changing environmental perceptions may be another strategy for depression prevention among older adults considering the sex differences. The present study had some limitations that should be noted. First, although the depression scale was dichotomous (mitigating vague responses) and specifically designed for older adults, this method is not always consistent with clinical diagnoses. Second, the measurements for personal, behavioral, and environmental factors were self-reported, so they might have been subject to recall bias or under-reported because of the stigma attached to them.<sup>51</sup> Furthermore, we did not control some potential confounders such as previous medical history and cognitive or functional impairment, which might have confounded the associations. Future related studies should take into account these variables. Third, the study was cross-sectional in design; thus, it could not prove causal relationships. Finally, the study might not be representative of the overall population, because the segment of the population without a household telephone (approximately 7.1% in 2015) was unreachable.<sup>52</sup> In addition, selection bias might have caused the proportion of men aged 75 and above more than women and the prevalence of depression in the present study to be much higher than the official statistics.<sup>53</sup>

## Conclusion

In addition to self-rated health, sex differences in the associations between factors and depression were observed in older adults. Encouraging men to spend more time on leisure walking and modifying a safe traffic environment while

advocating women to spend less time on TV watching were associated with lower risks of depression among older adults.

## Abbreviations

OR, odds ratio; GDS-4, Geriatric Depression Scale-4; BMI, body mass index; IPAQ, International Physical Activity Questionnaire; IPAQ-E, International Physical Activity Questionnaire Environmental Module; CIs, confidence intervals.

## Ethics approval and informed consent

We obtained verbal informed consent from the participants. The study protocols were reviewed and approved by the Ethics Committee of National Taiwan Normal University (201605HM006).

## Data availability

The data used during the present study are available from the corresponding authors upon reasonable request.

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## Author contributions

All authors contributed towards data analysis, drafting and critically revising the paper, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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