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The Mediating Role of Depressive Symptoms and Treatment Burden on Health-Related Quality of Life Among Multimorbid Patients With Hypertension: A Multi-Group Analysis

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Received: 27 June 2024 | **Accepted:** 27 September 2024

Funding: This work was supported by a National Research Foundation of Korea grant funded by the Korean government [grant number: 2021R1C1C100849812].

Keywords: comorbidity | depressive symptoms | health-related quality of life | multi-group analysis | multimorbidity | multimorbidity treatment burden

ABSTRACT

Multimorbidity negatively affects health-related quality of life (HRQoL), though the underlying mechanism remained unclear. This study aims to investigate the mediating role of depressive symptoms and multimorbidity treatment burden (MTB) in the association between disease burden and HRQoL in multimorbid patients with hypertension and to determine differences in mediating effects between and within age groups (< 60 years vs. 60 and above). Disease burden, depressive symptoms, MTB, and HRQoL were assessed by self-reported questionnaires. We conducted path analysis with all subjects and multi-group path analyses with two age groups. Results from the path analysis with all subjects ($n = 498$) showed a significant direct effect of disease burden on HRQoL and a significant indirect effect via depressive symptoms and MTB. No significant differences in mediating effects were found between age groups. However, in the older patients, depressive symptoms had a greater indirect effect than MTB. Our results underscore the importance of addressing both depressive symptoms and MTB in interventions tailored to the patient's age.

1 | Introduction

Multimorbidity, which is defined as the coexistence of multiple diseases (Johnston et al. 2019), poses a significant challenge to public health, with an estimated global prevalence of 37.2% (Chowdhury et al. 2023). This figure is expected to increase as populations age worldwide (Nguyen et al. 2019). Among individuals with multimorbidity, hypertension emerged as the most prevalent chronic condition (Miranda et al. 2019; Pati et al. 2015). Additionally, the combination of hypertension and hyperlipidemia was reported as the most frequent multimorbidity pair (Schiltz 2022).

Researchers have highlighted the negative impact of multimorbidity on health outcomes (Makovski et al. 2019; Pati et al. 2015; Skou et al. 2022). To address this impact, a core outcome set was developed, and health-related quality of life (HRQoL) was suggested as an essential patient-reported outcome in multimorbidity (Smith et al. 2018). Although the challenges of estimating the pooled effect of multimorbidity on HRQoL were described due to the heterogeneity in multimorbidity measures (e.g., the disease counts and sum of the weighted scores) or definitions (Nguyen et al. 2019), recent meta-analyses indicated an adverse association between a greater number of chronic conditions and HRQoL as well as

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Summary

- This study found that depressive symptoms and multimorbidity treatment burden mediated the relationship between disease burden and health-related quality of life in multimorbid patients with hypertension, irrespective of age.
- We also found within-group differences in older adults, showing greater mediating effects of depressive symptoms compared to multimorbidity treatment burden.
- This study highlights the importance of considering aging when designing interventions to enhance health-related quality of life in multimorbid patients with hypertension.

changes in HRQoL (Butterly et al. 2023; Makovski et al. 2019). Therefore, developing effective strategies to mitigate these effects is crucial, with a preliminary focus on understanding the underlying mechanisms. However, previous studies have not fully investigated the mechanism of how multimorbidity affects HRQoL.

2 | Background

The relationship between depressive symptoms and HRQoL has been well-researched in patients with chronic diseases, such as patients with chronic obstructive pulmonary disease or diabetes mellitus (Blakemore et al. 2014; Jing et al. 2018). Consistently, depressive symptoms were negatively associated with HRQoL in patients with multimorbidity (Gallegos-Carrillo et al. 2009; She et al. 2019). Patients with multimorbidity were twice as likely to experience depressive symptoms than those with a single disease (Read et al. 2017). Treatment burden is defined as the perceived effort patients need to care for their health and the impact on their well-being (Eton et al. 2012). Patients with multimorbidity experience treatment burden from simultaneously managing multiple chronic conditions including following recommended therapeutic regimens for multiple chronic diseases and their emotional distress from managing the necessary healthcare tasks (i.e., multimorbidity treatment burden, MTB). MTB from multiple chronic conditions has been associated with poor HRQoL in patients with multimorbidity (Eton et al. 2017; Gebreyohannes et al. 2023) and multimorbidity management guidelines recommend reducing treatment burden (Boyd et al. 2019; Leppin, Montori, and Gionfriddo 2015; Vetrano et al. 2017). Therefore, it is possible that depressive symptoms and MTB can mediate the relationship between multiple chronic conditions and HRQoL in this population.

Age should be considered when examining the mediating effect of depressive symptoms and MTB on the relationship between multimorbidity and HRQoL. As people age, they tend to prioritize emotionally meaningful goals over future-oriented goals such as expanding social networks (Carstensen, Fung, and Charles 2003). Although depressive symptoms are less prevalent in older adults than in younger adults (Fiske, Wetherell, and Gatz 2009), this shift in goals among older adults can lead to severe consequences of being depressed (Fiske, Wetherell, and Gatz 2009). These age-related differences in social goal prioritization can contribute to variations in how depressive symptoms and MTB mediate the relationship between multimorbidity and HRQoL between older and younger patients who have multiple chronic conditions.

Therefore, we hypothesized that the mediating effects of depressive symptoms and MTB in the relationship between multimorbidity and HRQoL would differ by age.

The purpose of this study was to investigate the relationships among multimorbidity, depressive symptoms, MTB, and HRQoL. The specific aims of this study were to (1) explore the mediating effect of depressive symptoms and MTB in the relationship between multimorbidity measured with disease burden and HRQoL in multimorbid patients with hypertension; and (2) determine whether there is a difference in mediating effects within each age group (younger and older patients) and between the two age groups (Figure 1). Our sample was limited to patients with hypertension who had at least two co-existing conditions. The characteristics of our sample reflect those of many patients with multimorbidity because hypertension often coexists with both pathophysiologically related and unrelated conditions (Unger et al. 2020), and hypertension is the most common condition for patients with multimorbidity (Miranda et al. 2019; Pati et al. 2015). The negative association between multiple chronic conditions and HRQoL has been reported in patients with hypertension (Mannan et al. 2022), which is also consistent with previous studies focusing on patients with multimorbidity (Makovski et al. 2019; Pati et al. 2015; Skou et al. 2022). We also measured multimorbidity with disease burden. This is a subjective burden from comorbidities reflecting disease severity because the subjective concept of disease burden has been considered more pertinent to HRQoL, and the common measure of disease count has faced criticism in terms of its inadequacy to reflect disease severity (Huntley et al. 2012; Makovski et al. 2019).

3 | Methods

3.1 | Study Design and Participants

This study used a cross-sectional design in which patients with hypertension and at least two other comorbidities were recruited from an online panel who voluntarily registered to participate in the survey. The inclusion criteria were as follows: (1) aged 19 years or older; (2) diagnosed with hypertension by clinicians

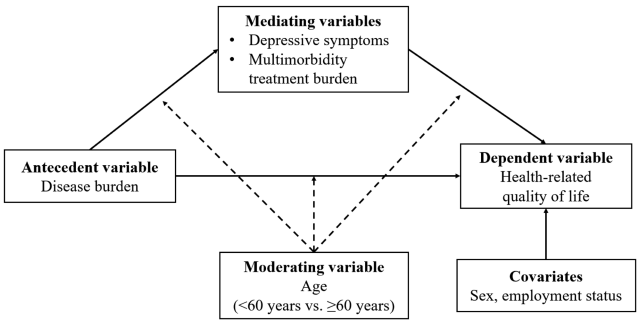


FIGURE 1 | The conceptual framework.

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and/or currently taking antihypertensive medications; (3) diagnosed with at least two other chronic diseases; and (4) able to read and speak Korean.

3.2 | Procedure

This study is a secondary data analysis of the baseline data in a longitudinal study aimed at evaluating the psychometric properties of a newly developed measure of the MTB (i.e., Treatment Burden for Multimorbidity Scale) in patients with hypertension and at least two comorbidities. Given that this study used secondary data, it was granted an exemption by the Institutional Review Board (IRB) at Seoul National University (IRB No. E2311/001–002). The data collection in the parent study was performed by sending invitation e-mails with recruitment documents to online panels. Participants answered questions for eligibility screening after they read the purpose and process of the study in the recruitment document and expressed their willingness to participate in the study. The participants who met the inclusion criteria were asked to sign an informed consent form and complete the questionnaire.

3.3 | Measures

3.3.1 | Disease Burden

Disease burden is defined as the subjective burden patients with chronic conditions experience, which reflects the limitations in their daily lives due to the severity of each condition (Bayliss, Ellis, and Steiner 2005). We measured disease burden using a self-reported subjective assessment of comorbidity burden developed by Bayliss and colleagues (Bayliss, Ellis, and Steiner 2005). However, we replaced the original list of chronic diseases by Bayliss and colleagues (Bayliss, Ellis, and Steiner 2005) with the list developed by Fortin and colleagues (Fortin, Almirall, and Nicholson 2017). Fortin and colleagues developed the list of 20 chronic diseases with a free text option for one additional condition by generating the initial 131 conditions from a scoping review of 33 publications on multimorbidity. They selected the chronic conditions based on four criteria: relevance and prevalence in a primary care setting, the impact on patients, and the prevalence found in the scoping review. The final list was then reviewed by 12 researchers (Fortin, Almirall, and Nicholson 2017). Meanwhile, the original list by Bayliss and colleagues included 25 chronic conditions, which were identified based on how often they had been investigated in studies on comorbidity (9 studies included), and the psychological condition (i.e., depression) was excluded from the list (Bayliss, Ellis, and Steiner 2005). Thus, due to these restrictions, we selected the list by Fortin and colleagues that was compiled based on comprehensive disease selection criteria.

To measure disease burden, patients were asked to rate the level of interference with daily activities caused by each of their conditions using a 5-point Likert scale (1 = "not at all" and 5 = "a lot") (Bayliss, Ellis, and Steiner 2005). The total score was calculated as the sum of all responses and ranged from 1 to 105. A higher score indicates a higher level of disease burden. The total score was derived using Fortin and colleagues' recommendation that a body mass index of 25 or higher be used to determine obesity (Fortin, Almirall, and Nicholson 2017).

3.3.2 | Depressive Symptoms

Depressive symptoms were measured by the nine-item Patient Health Questionnaire. Items are equivalent to the criteria of major depression in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Kroenke, Spitzer, and Williams 2001; Spitzer et al. 1999). Participants were asked to rate each of the items on how often a symptom bothered them over the last two weeks. Each item was rated with a four-point Likert scale ranging from 0 ("not at all") to 3 ("nearly every day"). Total scores were calculated as the sum of all responses and ranged from 0 to 27, with a higher score indicating a higher level of depressive symptoms. The degree of depressive symptoms was categorized based on the score of the nine-item Patient Health Questionnaire as follows: 0–4 (no depressive symptoms), 5–9 (mild depressive symptoms), 10–14 (moderate depressive symptoms), 15–19 (moderately-severe depressive symptoms), and 20–27 (severe depressive symptoms) (Kroenke, Spitzer, and Williams 2001).

3.3.3 | MTB

The Treatment Burden for Multimorbidity Scale was used to measure the levels of MTB (Lee et al. 2023). This questionnaire was developed based on an extensive literature review including existing MTB instruments (e.g., the Multimorbidity Treatment Burden Questionnaire and the Patient Experience with Treatment and Self-management), and validated with hypertensive patients with comorbidities (Lee et al. 2023). This questionnaire includes 12 items consisting of two subdomains (i.e., workload from healthcare tasks [8 items] and the impact on patients' lives [4 items]). Each item was rated on a 5-point Likert scale (Lee et al. 2023). After summing the items in each subdomain, the scores were standardized to 100. Total scores were the average of the two subdomain scores and ranged from 0 to 100, with a higher total score indicating a greater level of MTB. The Cronbach's alpha of the Treatment Burden for Multimorbidity Scale was 0.93 in this study.

3.3.4 | HRQoL

HRQoL was measured with the Patient-Reported Outcomes Measurement Information System-29 profile v2.1 (PROMIS-29 v2.1) (Hays et al. 2018). This questionnaire includes eight domains: physical function, anxiety/fear, depression/sadness, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference, and pain intensity. Each domain was scored based on a T-score transforming the raw score into a standardized score with a mean of 50 and a standard deviation of 10. Because the total scores of the PROMIS-29 v2.1 were not available, we used the PROMIS-Preference scores (Dewitt et al. 2018). Scores were a single preference-based summary score computed with scores of the seven domains of PROMIS-29 v2.1 excluding pain intensity and imputing scores of the cognition domain predicted by the linear regression model suggested

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by Klapproth and colleagues (Klapproth et al. 2022). The PROMIS-Preference scores can range from −0.022 to 1 (Dewitt et al. 2018). A higher score means better health status and a negative score means worse health than dead status (Dewitt et al. 2018). The PROMIS-Preference scores were validated in a large sample of the general US population with good construct validity (Hanmer et al. 2018).

3.3.5 | Socio-Demographic and Clinical Variables

Participants were asked to report socio-demographic information (e.g., age, gender, education level, and employment status) and clinical information (e.g., number of comorbidities and the number of medication types they took over the past 3 months). In this study, the entire sample was divided into those who were under 60 years (i.e., younger patient group) and those who were 60 years and above (i.e., older patient group) based on the retirement age in Korea.

3.4 | Statistical Analyses

Descriptive statistics were used to describe the sample characteristics. Independent samples t-tests, chi-square tests, and Fisher's exact tests were performed to examine the differences in socio-demographic and clinical characteristics between the younger and older patient groups. The analyses were conducted using IBM SPSS version 26.0.

Path analysis was performed to examine the mediating role of depressive symptoms and MTB on the relationship between disease burden and HRQoL with all subjects. A previous study reported a correlation between mental health (e.g., depression and anxiety) and high MTB (Eton et al. 2019; Sav et al. 2016). Thus, we set a correlation between the errors of depressive symptoms and MTB. We also adjusted for gender and employment status because female or unemployed people with multimorbidity reportedly have poorer HRQoL than their male or employed counterparts (Makovski et al. 2019; Park et al. 2018).

Multi-group analysis was also conducted to determine the differences in direct and indirect effects within and between the two age groups (younger vs. older patient groups) for the second aim of our study. Kline recommended using unstandardized estimates to determine the differences in path estimates and mediating effects between age groups, while standardized estimates should be used to examine the within-group difference, accounting for the different units of scales of indicators (Kline 2016). The goodness-of-fit of the model was assessed based on the following criteria: p-value of chi-square test > 0.05, comparative fit index (CFI) and Tucker-Lewis index (TLI) ≥ 0.95, root mean square error of approximation (RMSEA) < 0.08, and standardized root mean square residual (SRMR) < 0.08 (Browne and Cudeck 1992; Hu and Bentler 1999). The significance levels of the independent samples t-tests, chi-square tests, and path estimates of mediation analyses were set at p-value < 0.05. The significance of direct and indirect effects and differences in direct and indirect effects within and between age groups was determined by examining the bootstrap confidence intervals using 10 000 bootstrap samples. The mediation analyses were conducted using Mplus 8.8.

4 | Results

4.1 | Participant Characteristics

A total of 498 patients were included in this study: 70.3% under the age of 60, and 29.7% 60 and older (Table 1). The mean age of participants was 53.2 (SD = 10.4) years with younger 48.5 (SD = 8.5) years and older 64.3 (SD = 4.0) years. Compared to younger patients, the proportion of female and unemployed status was higher in older patients (all p-values < 0.05). The number of comorbidities was not different between the two age groups (a mean of 3.2 [SD = 1.4] in younger patients and a mean of 3.2 [SD = 1.2] in older patients). The most prevalent chronic conditions of younger patients were hyperlipidemia (68.9%), obesity (66.9%), diabetes mellitus (43.4%), and those of older patients were hyperlipidemia (66.2%), diabetes mellitus (41.2%), and obesity (40.5%). The proportion of patients taking five or more prescribed medications a day did not differ by age group.

The levels of disease burden did not differ by age group. However, younger patients reported greater levels of depressive symptoms, MTB, and lower levels of HRQoL than older patients (all p-values < 0.05). Based on the cutoff scores of 10 on the Patient Health Questionnaire, the proportion of patients experiencing moderate or severe levels of depressive symptoms was 106 (30.3%) in younger patients and 26 (17.6%) in older patients.

4.2 | Mediation Model with All Subjects

Figure 2 shows the path estimates and direct and indirect effects of the mediation model adjusted for gender and employment status with all subjects. The path estimates between all variables were significant except for gender and employment status (all $p < 0.05$). Disease burden had a direct effect on HRQoL ($B = -0.005$, $\beta = -0.147$, $p < 0.01$). The relationship between disease burden and HRQoL was mediated by depressive symptoms (unstandardized estimate = −0.007, 95% bootstrap confidence interval = [−0.009, −0.005], standardized estimate = −0.199), and MTB (unstandardized estimate = −0.005, 95% bootstrap confidence interval = [−0.007, −0.004], standardized estimate = −0.157). The 65.6% of the variance of HRQoL was explained in this model. The model fit indices of the overall mediation model were satisfactory: χ^2 ($df = 4$) = 2.609, $p = 0.625$, CFI = 1.000, TLI = 1.000, RMSEA = 0.000, SRMR = 0.020.

4.3 | Multi-Group Mediation Analyses by Age Group

Table 2 presents the parameter estimates of multi-group mediation models adjusted for gender and employment status. In the younger patient group, the direct effect of disease burden on HRQoL ($B = -0.004$, $\beta = -0.128$, $p < 0.01$) and the indirect effects via depressive symptoms (unstandardized estimate = −0.006),

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TABLE 1 | Participants' characteristics ($n = 498$).

Characteristics	All subjects ($n = 498$)	< 60 years ($n = 350$)	≥ 60 years ($n = 148$)	*p*
	Frequency (%) or Mean (SD)			
Age, year	53.2 (10.4)	48.5 (8.5)	64.3 (4.0)	< 0.001
Gender				0.006
Male	374 (75.1)	275 (78.6)	99 (66.9)	
Female	124 (24.9)	75 (21.4)	49 (33.1)	
Education level				0.212
Lower than high school graduation	3 (0.6)	1 (0.3)	2 (1.4)	
At or higher than high school graduation	495 (99.4)	349 (99.7)	146 (98.6)	
Employment status				< 0.001
Full or part-time	370 (74.3)	294 (84.0)	76 (51.4)	
Unemployed	128 (25.7)	56 (16.0)	72 (48.6)	
Number of comorbidities	3.2 (1.3)	3.2 (1.4)	3.2 (1.2)	0.783
Years since the hypertension diagnosis	8.4 (7.1)	7.3 (6.3)	11.1 (8.2)	< 0.001
Taking five or more prescribed medications a day ($n = 497$)	98 (19.7)	71 (20.3)	27 (18.2)	0.590
Disease burden	11.0 (6.3)	11.3 (6.4)	10.3 (6.0)	0.102
Depressive symptoms	6.7 (5.8)	7.4 (6.1)	4.8 (4.7)	< 0.001
Multimorbidity treatment burden	37.2 (22.5)	39.2 (22.7)	32.4 (21.4)	0.002
Health-related quality of life	0.40 (0.21)	0.38 (0.21)	0.47 (4.75)	< 0.001

Note: SD: Standard deviation.

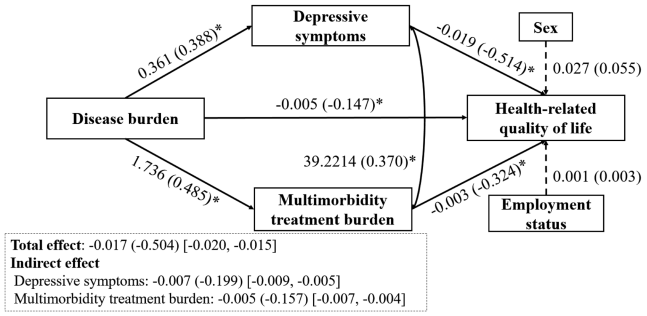


FIGURE 2 | The results of mediation analysis with all subjects. *$p < 0.05$, The estimates are presented as standardized estimates (unstandardized estimates). The brackets indicate unstandardized 95% bootstrap confidence intervals. Solid lines indicate paths with significant estimates. The model fit indices are satisfactory.

95% bootstrap confidence interval = [−0.008, −0.004] and MTB (unstandardized estimate = −0.006, 95% bootstrap confidence interval = [−0.008, −0.004]) were significant after adjusting for gender and employment status with an R^2 of 0.680. In the older patient group, the direct effect of disease burden on HRQoL ($B = -0.006$, $\beta = -0.180$, $p = 0.02$) and the indirect effects via depressive symptoms (unstandardized estimate = −0.008, 95% confidence interval = [−0.012, −0.005]) and MTB (unstandardized estimate = −0.004, 95% confidence interval = [−0.006, −0.001]) were also significant after adjusting for gender and employment status. The R^2 of HRQoL in the older patient group was 0.586.

When the differences in the paths between the two age groups were tested, the path of depressive symptoms to HRQoL was greater in the older patient group than in the younger patient group (difference = 0.006, $p = 0.04$). No significant differences were found in the estimates of the following paths: disease burden to depressive symptoms and MTB, and MTB to HRQoL. In addition, there were no significant differences between the two age groups in the direct effect path of disease burden to HRQoL and indirect effect paths via depressive symptoms and MTB.

In the within-group difference analyses, the standardized indirect effects through depressive symptoms and MTB were not different in the younger patient group (difference = −0.002, 95% bootstrap confidence interval = [−0.081, 0.074]). However, in the older patient group, the standardized indirect effect via

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TABLE 2 | Differences in parameter estimates of a direct and indirect effect based on age.

Path	Age group		Differences in the effects between groups
	<60 years ($n=350$)	≥60 years ($n=148$)	
Disease burden → depressive symptoms	0.349*	0.347*	0.002
Disease burden → multimorbidity treatment burden	1.782*	1.509*	0.272
Depressive symptoms → HRQoL	−0.017*	−0.024*	0.006*
Multimorbidity treatment burden → HRQoL	−0.003*	−0.002*	−0.001
Direct effect			
Disease burden → HRQoL	−0.004*	−0.006*	0.002
Indirect effect			
Disease burden → depressive symptoms → HRQoL	−0.006 [−0.008, −0.004]	−0.008 [−0.012, −0.005]	0.002 [−0.002, 0.007]
Disease burden → multimorbidity treatment burden → HRQoL	−0.006 [−0.008, −0.004]	−0.004 [−0.006, −0.001]	−0.003 [−0.006, 0.001]
Differences in indirect effects within the group	−0.002 [−0.081. 0.074]	0.131 [0.020, 0.258]*	

Note: HRQoL: Health-related quality of life. The brackets indicate 95% bootstrap confidence intervals. Asterisks (*) indicate the significant estimates based on $p<0.05$ or the 95% bootstrap confidence intervals. Except for the difference in indirect effects within group reported by standardized estimates, all other parameter estimates were reported based on unstandardized estimates (Kline 2016). Models were adjusted for gender and employment status.

depressive symptoms was greater than that via the MTB (difference = 0.131, 95% bootstrap confidence interval = [0.020, 0.258]). The model fit indices of the multi-group mediation model were χ^2 ($df=8$) = 0.887, $p=0.100$, CFI = 1.000, TLI = 1.000, RMSEA = 0.000, and SRMR = 0.011.

5 | Discussion

We found that depressive symptoms and MTB mediated the relationship between disease burden and HRQoL in multimorbid patients with hypertension. The findings of the multi-group analyses indicated nonsignificant between-group differences in the mediating effects of depressive symptoms and MTB on the relationship between disease burden and HRQoL. However, within-group differences were evident in the older patient group, with a greater indirect effect via depressive symptoms than via MTB.

Studies have suggested that HRQoL is an essential outcome in patients with multimorbidity (Smith et al. 2018). Thus, significant efforts have been made to improve HRQoL in this population. However, recent systematic reviews including the Cochrane review (Eriksen et al. 2022; Smith et al. 2021) have indicated that intervention studies reporting HRQoL as a primary outcome did not yield improvements in HRQoL. The lack of positive effects from these interventions on HRQoL could be partially attributed to an incomplete understanding of the mechanism of how multimorbidity affects HRQoL.

We found that worsening HRQoL from multiple chronic conditions was related to increasing depressive symptoms and MTB. However, studies (Kamradt et al. 2019; Salisbury et al. 2018; Schäfer et al. 2018) focusing on HRQoL as a primary endpoint did not include strategies targeting both depressive symptoms and MTB, particularly in studies where mental disorders were not targeted chronic conditions (Eriksen et al. 2022). None of these studies (Kamradt et al. 2019; Salisbury et al. 2018; Schäfer et al. 2018) addressed and managed patients' emotional states including depressive symptoms, even though depressive symptoms are prevalent in patients with multimorbidity (Read et al. 2017) included in our study (26.5% of patients had moderate to severe depressive symptoms). One previous study also showed that depressive symptoms mediated the relationship between multimorbidity measured with the disease count and HRQoL in 1497 patients aged 60 and older, accounting for about 83% of people with multimorbidity (She et al. 2019).

In studies focusing on the HRQoL of patients with multimorbidity (Kamradt et al. 2019; Salisbury et al. 2018; Schäfer et al. 2018), common approaches to alleviate MTB involve medication reviews and individualized care planning incorporating patients' preferences and goals. These approaches align with guidelines for the care of patients with multimorbidity (Boyd et al. 2019; Leppin, Montori, and Gionfriddo 2015; Vetrano et al. 2017). However, Salisbury and colleagues' unexpected findings showed that implementing their guideline-based, well-designed patient-centered model did not result in reduced MTB and did not improve HRQoL (Salisbury et al. 2018). Notably, Salisbury and colleagues' (Salisbury et al. 2018) study was the only one reporting MTB, and, surprisingly, strategies aimed at reducing MTB were not effective. A possible explanation could be that the interventions did not include patient education and skill-building components on how to incorporate care planning

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in patients' daily routines and how to mobilize or coordinate resources to perform healthcare tasks. These components have been described as essential to decrease patients' MTB (Shippee et al. 2012).

According to the socioemotional selectivity theory (Carstensen, Fung, and Charles 2003), individuals' perceptions of how much time they have left affects their prioritization of social goals. Older adults who tend to perceive that their time is limited prioritize emotionally meaningful goals to maximize life satisfaction and emotional well-being (Carstensen, Fung, and Charles 2003). In contrast, young adults who tend to perceive that they have a longer time prioritize future-oriented goals such as pursuing knowledge acquisition and career development. Even when faced with stressful situations such as diagnoses of additional chronic conditions, older adults can cope with the situation a little more smoothly through a positive reappraisal of the event compared to younger adults (Carstensen, Fung, and Charles 2003). Consistent with this theory, we found that the older patient group experienced lower levels of depressive symptoms and MTB and higher levels of HRQoL compared to the younger patient group, which also aligned with previous studies on multimorbidity (Herzig et al. 2019; Makovski et al. 2019; Read et al. 2017).

We also found no significant difference in the mediating effect of depressive symptoms and MTB between younger and older patient groups. This finding suggests that both depressive symptoms and MTB are pivotal mechanisms in explaining the relationship between multimorbidity and HRQoL, irrespective of age. However, we identified a difference in the older patient group: the mediating effect of depressive symptoms was greater than that of the MTB. This finding indicates that older multimorbid patients with hypertension were particularly susceptible to a decline in HRQoL when they experienced depressive symptoms compared to when they were burdened with healthcare tasks managing multiple chronic conditions. This observation can be further explained by the socioemotional selectivity theory (Carstensen, Fung, and Charles 2003). Older adults experiencing depressive symptoms may compromise their psychological resilience (less reactive to negative stimuli) as they make emotional well-being a top priority as they recognize that they have limited time remaining. Therefore, it is critical for clinicians and researchers to understand age-related differences and tailor interventions with different emphasis on depressive symptoms and MTB for each age group in order to effectively improve HRQoL.

There were several limitations in this study. First, the generalizability of our study is limited because the parent study employed convenience sampling from an online panel. Although we were able to access a variety of potential participants irrespective of where they lived, the participants had relatively fewer chronic conditions compared to samples in other studies on multimorbidity. We were unable to recruit a wide range of older people from an online panel as the range of the older patient group was 60 to 82 years old, even though the internet usage rate of elderly people in South Korea is high at 83.7% (National Information Society Agency 2022). The education levels in Korea are also higher than the average of Organization for the Economic Cooperation and Development countries, and national data indicate that 89% of Koreans aged 25 to 64 years have completed at least a high school education (Organization for the Economic Cooperation and Development countries 2023). Therefore, the relatively higher education levels of our sample are reflective of the national trends. Nevertheless, due to these limitations, further research is needed to recruit a representative sample. Second, the psychometric property of the disease burden measure with a modified list of chronic conditions we used was limited. Although the list of chronic conditions developed by Fortin and colleagues (Fortin, Almirall, and Nicholson 2017) was comprehensive and reflected the prevalent chronic conditions in Korea, more studies are needed to support the psychometric soundness of the disease burden measure with a modified list of chronic conditions. Finally, our study only included multimorbid patients with hypertension, which may not reflect the characteristics of multimorbid patients with different disease combinations.

6 | Conclusions

Improving HRQoL is important in the management of multimorbidity. However, previous intervention studies focusing on HRQoL have not shown significant improvements in HRQoL in patients with multimorbidity. To develop effective interventions, our study explored the potential mechanisms of how multimorbidity may affect HRQoL. Our findings revealed that depressive symptoms and MTB serve as mediators in the relationship between multimorbidity measured with disease burden and HRQoL in multimorbid patients with hypertension. We also found that the impact of multimorbid disease burden on HRQoL is more pronounced when mediated by depressive symptoms than MTB in older adults. These findings underscore the need to simultaneously address depressive symptoms and MTB in interventions and to tailor the emphasis of the interventions based on the patients' age groups. However, as our study focused specifically on multimorbid patients with hypertension, further research is warranted to broaden our understanding of these relationships to encompass a more diverse population with multimorbidity.

7 | Relevance for Clinical Practice

Patients with multimorbidity tend to experience a lower HRQoL than patients with a single disease. Identifying the mechanisms by which multimorbidity affects HRQoL is critical to improving the HRQoL of patients with multimorbidity. We found that depressive symptoms and MTB mediated the relationship between multimorbidity and HRQoL. We also found that the mediating effect of depressive symptoms was greater than that of depressive symptoms in older adults. Our findings suggest that healthcare providers need to develop interventions that address both depressive symptoms and MTB to improve HRQoL in patients with multimorbidity, while also considering patients' aging.

Author Contributions

Jihyang Lee: conceptualization, methodology, software, data curation, investigation, formal analysis, visualization, writing – original draft.

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Su-Young Kim: methodology, software, formal analysis, writing – review and editing. **Kyoung Suk Lee:** conceptualization, methodology, software, data curation, investigation, validation, formal analysis, supervision, funding acquisition, writing – original draft, project administration, writing – review and editing.

Acknowledgments

This study was supported by a National Research Foundation of Korea grant funded by the Korea government (2021R1C1C100849812). Jihyang Lee received a scholarship from the BK21 education program (Center for World-leading Human-care Nurse Leaders for the Future).

Ethics Statement

The IRB of the Seoul National University has confirmed that no ethical approval is required (IRB No. E2311/001-002). The data collection for the parent study was performed after obtaining IRB approval from Seoul National University (IRB No. 2306/001-012).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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