

# Factors Associated with Medication-Related Burden Quality of Life (MRB-QoL) in Community-Dwelling Adults with Long-Term Conditions: An Exploratory Study

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**Background:** The Medication-Related Burden Quality of Life (MRB-QoL) tool has been developed to measure the burden of medications on functioning and wellbeing from a patient perspective. However, predictors of MRB-QoL were not reported in greater detail in the validation study. This study aimed to explore factors associated with MRB-QoL to see whether there is any new information that calls for further research.

**Methods:** Analysis of data from the MRB-QoL validation study was undertaken. Outcome variables were domains of the MRB-QoL (Routine and Regimen Complexity, Psychological Burden, Functional and Role Limitation, Therapeutic Relationship, and Social Burden). Explanatory variables were patient age; disease-related factors; and medication-related factors, such as number of medications, complexity of medication regimen (measured by the Medication Regimen Complexity Index [MRCI]), and exposure to medications with anticholinergic and sedative effects (measured by the Drug Burden Index [DBI]). Linear regression analyses were used to identify factors associated with the MRB-QoL.

**Results:** The study included 367 participants (52.1% male), with a median age of 64 years. In multivariable regression analyses, an increase in the DBI was significantly associated with poorer Psychological wellbeing ( $\beta=-0.15$ ,  $p<0.001$ ) and Functional and Role Limitation ( $\beta=-1.79$ ,  $p<0.001$ ). Living with three or more medical conditions was significantly associated with poorer Psychological wellbeing ( $\beta=-0.21$ ,  $p<0.001$ ). Age was significantly associated with all domains of the MRB-QoL ( $\beta=0.28$  to  $0.55$ ). Polypharmacy and MRCI were not associated with any of the MRB-QoL domains.

**Conclusion:** In this sample of community-dwelling adults with multiple medications, the DBI was independently associated with the Psychological Burden and Functional and Role Limitation domains of the MRB-QoL. This study provides preliminary evidence on factors affecting medication-related quality of life outcomes from a patient perspective. Future longitudinal studies, along with further psychometric testing of the MRB-QoL measure, are warranted to better understand predictors of MRB-QoL.

**Keywords:** patient-reported outcomes, medication-related burden, quality of life, community-dwelling adults

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## Introduction

Advances in medicine and public health coupled with improved living standards have significantly contributed to reductions in mortality and increased life expectancy.<sup>1-3</sup> However, with longevity, most patients live with multiple chronic

diseases and medications. With appropriate use, medicines improve patients' health outcomes, overall well-being, and functioning. However, there are often negative consequences associated with the long-term use of medicines. These may include adverse events, the burden on day-to-day life, and the impact on social, financial, psychological, and functional well-being.<sup>4-8</sup>

Health-related quality of life (HRQoL) is an essential treatment goal in pharmacotherapeutic interventions. However, most widely used HRQoL measures are not sensitive enough to detect the changes in HRQoL related to pharmacotherapy.<sup>8</sup> Thus far, only a few measures, such as the Patient-Reported Outcomes Measure of Pharmaceutical Therapy for Quality of Life (PROMPTQoL),<sup>9</sup> Medication-Related Quality of Life (MRQOL),<sup>10</sup> and Medication-Related Burden Quality of Life (MRB-QoL),<sup>11</sup> combining the concept of medication therapy and quality of life have been developed. It has been reported that all of these measures have good initial psychometric properties, yet they have not been widely used in the actual evaluation of the impact of pharmaceutical care (PC) interventions on medication-related quality of life outcomes. Previous studies that have evaluated HRQoL in relation to polypharmacy,<sup>12,13</sup> regimen complexity,<sup>13</sup> or pharmacological class of medication<sup>14-17</sup> have done so using HRQoL measures developed based on chronic disease models, not on drug therapy models. This could be partly because medication-specific measures of quality of life suitable for research purposes have not been developed or are in the early stages of development. However, a large body of evidence shows that although several factors affecting HRQoL have been evaluated using generic or disease-specific measures of HRQoL, the medication-specific burden on patients' well-being<sup>18</sup> cannot be captured using measures of HRQoL developed based on chronic disease models.<sup>19</sup> Furthermore, in the validation study of the MRB-QoL measure, predictors of medication-related quality of life outcomes were not reported in greater detail. In this study, we used regression analysis to further explore the relationship between the MRB-QoL tool and predictors measured in the MRB-QoL validation study<sup>11</sup> to see whether there is any new information that calls for further research.

## Methods

### Study Population

The present study focused on secondary analyses of data collected for validation of the MRB-QoL tool<sup>11</sup> to identify factors associated with the MRB-QoL measure. The

MRB-QoL study was conducted in Sydney, Australia, and data were collected from community-dwelling adults living with chronic conditions and taking multiple medications on a regular basis.<sup>11</sup> The sample size was estimated based on the ratio of responses per item of the MRB-QoL measure. The link to the MRB-QoL survey was distributed to potential participants. Screening questions were used to allow only eligible participants to complete the questionnaire. Participants were asked to indicate on a five-point Likert scale the extent to which they agreed or disagreed with each statement of the MRB-QoL measure, where 1= "strongly agree", 2= "agree", 3= "neither agree nor disagree", 4= "disagree", and 5= "strongly disagree". In addition, "prefer not to answer" was included as an alternative option to respect participants' choice of not responding to a given item. A two-week recall period was used to help participants recall relevant experience associated with medication burden. In total, 367 participants enrolled in the MRB-QoL study. A detailed description of the sample and methods can be found elsewhere.<sup>11</sup>

### Study Variables Outcome Measure

Domains of the MRB-QoL were used as an outcome variable. MRB-QoL is a patient-reported outcome measure of the burden of medicine on functioning and well-being. It has 31 items divided into five domains: Routines and Regimen Complexity (RRC), Psychological Burden (PsyB), Functional and Role Limitation (FRL), Therapeutic Relationship (TR), and Social Burden (SB). All domains of the MRB-QoL have good validity (construct, convergent/divergent, and known groups) and internal consistency reliability (range 0.87-0.95).<sup>11</sup>

### Explanatory Variables Medication Factors

Information about medication use was collected as part of the MRB-QoL tool validation. In the MRB-QoL validation study, participants were asked to provide details of medications, such as name, strength/dose, and number of times a day. The polypharmacy definition of five or more medications<sup>13,20,21</sup> was used to explore differences among participants based on the number of medications. The use of the anticholinergic and sedative class of medications was quantified using the Drug Burden Index (DBI).<sup>15</sup> The DBI is a measure of an individual's exposure to medications with anticholinergic and sedative effects

based on the principle of dose–response and maximum effect.<sup>15</sup> The burden of complexity of a medication regimen was quantified using the Medication Regimen Complexity Index (MRCI).<sup>22</sup> The MRCI is the sum of scores of dosage forms, frequency, and additional instructions.

### Chronic Disease Factors

Lists of chronic medical conditions were obtained from patient self-report in the MRB-QoL tool validation. The burden of comorbidities was quantified using the Charlson Comorbidity Index (CCI).

### Other Covariates

Age was the other independent variable included in the analysis.

## Statistical Analyses

Characteristics of the study participants were summarized using descriptive statistics. Normally distributed continuous data are presented as the mean and standard deviation. Non-normally distributed continuous data are presented as the median and interquartile range (IQR), whereas categorical variables are reported using frequencies and percentages. The MRB-QoL subscales comprised non-normally distributed continuous data and, thus, for linear regression analysis the data were transformed using a rank order method.<sup>23</sup> Tests for linear regression assumptions (linearity, homoscedasticity, normality, and multicollinearity) were conducted to evaluate the suitability of the data. Multicollinearity between each explanatory variable was assessed using tolerance and the variance inflation factor (VIF) (>10 threshold).<sup>24</sup> Univariate linear regression analysis was conducted to explore the association between the MRB-QoL subscales and each explanatory variable. Variables were retested in multivariable linear regression analyses. Stepwise multiple linear regression analyses were conducted to compare the relative contribution and influence of each explanatory variable on the outcome variables. Thus, medication, disease, and demographic factors were entered in the series of analyses model to explore the variance of MRB-QoL domains explained by each factor. Results are presented using regression coefficients (unstandardized and adjusted) and *p*-values, and the level of statistical significance was determined at a *p*-value <0.05. Analyses were conducted using SPSS version 22.

## Results

### Characteristics of Study Participants

In total, 367 patients were included in this study (52.1% male). The median numbers of chronic medical conditions and prescription medications were 3 and 5, respectively. Most respondents were on five or more medications (n=200) and living with three or more medical conditions (n=195). The proportion exposed to medication with anticholinergic and sedative effects (ie, DBI>0) was 52.9% (n=148). Detailed characteristics of the study participants are presented in [Table 1](#).

Analyses of transformed data showed no evidence of violation of the assumptions of linearity, normality, homoscedasticity, and multicollinearity. Visual inspection of scree plots of standardized residuals supported homoscedasticity and showed no significant outliers. There was no evidence of multicollinearity among independent variables (VIF=1, tolerance= 1).

## Regression Analyses

### Routine and Regimen Complexity (RRC) Domain

The mean score on the RRC domain was 25.2±10.52. In linear regression analyses, all variables were significantly associated with RRC scores except for MRCI (*p*=0.06) ([Table 2](#)). The association was stronger for age, DBI, and medical condition. For every unit increase in DBI, the RRC score decreased by 3.04 (*p*<0.01). Similarly, for every unit increase in the number of medications and medical conditions, the RRC score decreased by 0.87 (*p*<0.01) and 1.5 (*p*<0.01), respectively. In multivariable regression analyses, age was the only variable significantly associated with the RRC domain ([Table 3](#)). In a stepwise

**Table 1** Characteristics of Study Participants (N=367)

Variables	
Age (years), median (IQR)	64 (49–70)
Male gender, n (%)	188 (51.2)
Number of medical conditions (IQR)	3 (2–3)
Number of prescription medications (IQR)	5 (3–7)
Number of over-the-counter medications (IQR)	2 (1–3)
CCI (IQR)	3 (0–4)
MRCI (IQR)	9 (7–13)
Total DBI (IQR)	0.5 (0–0.9)
DBI >0 (IQR)	0.9 (0.7–1.6)
DBI =0, n (%)	132 (47.1)
DBI >0, n (%)	148 (52.9)

**Abbreviations:** CCI, Charlson Comorbidity Index; DBI, Drug Burden Index; IQR, interquartile range; MRCI, Medication Regimen Complexity Index.

**Table 2** Association of Demographic and Clinical Characteristics with MRB-QoL (N=367)

Variables	R <sup>2</sup>	β-Coefficient (Unstandardized)	p-Value
<b>Routine and regimen complexity (RRC)</b>			
DBI	0.23	-3.04	<0.01*
CCI	0.17	0.86	<0.01*
MRCI	0.11	-0.21	0.06
Number of medical conditions	0.21	-1.54	<0.01*
Number of medications	0.22	-0.87	<0.01*
Age	0.52	3.5	<0.01*
<b>Psychological Burden (PsyB)</b>			
DBI	0.26	-1.96	<0.01*
CCI	0.14	0.42	0.02*
MRCI	0.13	-0.14	0.03*
Number of medical conditions	0.23	-0.97	<0.01*
Number of medications	0.14	-0.32	0.01*
Age	0.32	0.12	<0.01*
<b>Functional and Role Limitation (FRL)</b>			
DBI	0.29	-2.53	<0.01*
CCI	0.19	0.64	<0.01*
MRCI	0.05	-0.06	0.39
Number of medical conditions	0.18	-0.87	<0.01*
Number of medications	0.19	-0.52	<0.01*
Age	0.41	0.18	<0.01*
<b>Therapeutic Relationship (TR)</b>			
DBI	0.05	-0.19	0.37
CCI	0.18	0.25	<0.01*
MRCI	0.03	0.02	0.61
Number of medical conditions	0.17	-0.35	<0.01*
Number of medications	0.20	-0.22	<0.01*
Age	0.43	0.08	<0.01*
<b>Social Burden (SB)</b>			
DBI	0.19	-1.02	<0.01*
CCI	0.23	0.47	<0.01*
MRCI	0.02	-0.02	0.74
Number of medical conditions	0.15	-0.44	<0.01*
Number of medications	0.13	-0.21	0.03*
Age	0.50	0.14	<0.01*

Note: \*p<0.05.

**Abbreviations:** CCI, Charlson Comorbidity Index; DBI, Drug Burden Index; MRB-QoL, Medication-Related Burden Quality of Life; MRCI, Medication Regimen Complexity Index; R<sup>2</sup>, regression coefficient.

regression analysis in which medication, medical condition, and age variables were sequentially entered into the model, medication-related factors (ie, DBI, MRCI, and number of medications) accounted for 8% of the variance in the RRC score. Adding medical condition-related factors (ie, CCI and number of medical conditions) and age to

the model increased the total variance to 32%, with age (β=0.37) being the only variable significantly associated with RRC score (Table 4).

### Psychological Burden (PsyB) Domain

The mean score on the PsyB domain was 19.7±6.01. In linear regression analyses, all variables were significantly associated with the PsyB domain (Table 2). The association was stronger for DBI and medical condition. For every unit increase in DBI, the PsyB domain score decreased by 1.96 (p<0.01). Similarly, for every unit increase in the number of medical conditions, the PsyB domain score decreased by 0.97 (p<0.01). In multiple linear regression analyses, age, DBI, and medical condition were significantly associated with the PsyB domain score (Table 3). After adjusting for medication, medical condition, and age variables, it was found that a unit increase in DBI and number of medical conditions indicated a decrease in the PsyB domain score by 1.5 and 0.21, respectively. Medication-related factors (ie, DBI, MRCI, and number of medications) accounted for 7% of the variance in the PsyB domain score. Adding medical condition-related factors (ie, CCI and number of medical conditions) and age to the model increased the variance to 16% (Table 4).

### Functional and Role Limitation (FRL) Domain

The mean score on the FRL domain was 19.3±6.98. In linear regression analyses, all variables were significantly associated with the FRL domain score except for MRCI (p=0.39) (Table 2). The association was stronger for DBI and medical condition. For every unit increase in DBI, the FRL score decreased by 2.53 (p<0.01). Similarly, for every unit increase in the number of medical conditions, the FRL score decreased by 0.87 (p<0.01). In multivariable regression analyses, DBI and age were the only factors significantly associated with FRL score (Table 3). After adjusting for confounding factors, for every unit increase in DBI and number of medical conditions, the FRL domain score decreased by 0.20. Medication-related factors (ie, DBI, MRCI, and number of medications) explained 10% of the variance in FRL score. Addition of medical condition-related factors (ie, CCI and number of medical conditions) and age to the model increased the variability in the FRL domain score to 21%. DBI and age were the two major variables contributing to FRL outcome (Table 4).

**Table 3** Predictors of Medication-Related Burden Quality of Life (MRB-QoL) (N=367)

Variables	Unstandardized $\beta$ -Coefficient	Standardized $\beta$ -Coefficient	95% CI	
<b>Routine and Regimen Complexity (RRC): <math>aR^2=0.32</math></b>				
DBI	-1.23	-0.09	-2.79	0.33
CCI	-0.44	-0.09	-0.43	0.02
MRCI	-0.20	-0.11	-1.11	0.23
Number of medical conditions	-0.15	-0.02	-1.29	1.00
Number of medications	-0.42	-0.10	-1.01	0.18
Age	0.37*	0.55*	0.29	0.45
<b>Psychological Burden (PsyB): <math>aR^2=0.16</math></b>				
DBI	-1.15*	-0.15*	-2.14	-0.16
CCI	0.02	0.01	-0.40	0.45
MRCI	-0.07	-0.07	-0.95	0.34
Number of medical conditions	-0.88*	-0.21*	-1.61	-1.50
Number of medications	0.15	0.07	-0.22	0.53
Age	0.11*	0.28*	4.13	0.01
<b>Functional and Role Limitation (FRL): <math>aR^2=0.21</math></b>				
DBI	-1.79*	-0.20*	-2.91	-0.68
CCI	-0.08	-0.02	-0.56	0.39
MRCI	0.01	0.01	-0.15	0.17
Number of medical conditions	-0.12	-0.03	-0.94	0.69
Number of medications	-0.31	-0.12	-0.73	0.11
Age	0.16*	0.37*	0.11	0.22
<b>Therapeutic Relationship (TR): <math>aR^2=0.20</math></b>				
DBI	0.22	0.05	-0.26	0.69
CCI	0.03	0.02	-0.18	0.23
MRCI	0.004	0.008	-0.06	0.07
Number of medical conditions	-0.14	-0.07	-0.48	0.21
Number of medications	-0.15	-0.13	-0.33	0.03
Age	0.08*	0.41*	0.05	0.10
<b>Social Burden (SB): <math>aR^2=0.26</math></b>				
DBI	-0.39	-0.07	-1.05	0.27
CCI	-0.02	-0.01	-0.30	0.26
MRCI	-0.03	-0.04	-0.12	0.07
Number of medical conditions	-0.22	-0.07	-0.70	0.27
Number of medications	-0.03	-0.02	-0.28	0.22
Age	0.13*	0.49*	0.09	0.17

**Notes:**  $\beta$ , regression coefficient (change in the MRB-QoL domain in relation to the independent variables in the model adjusted by the rest of the covariates). \*Indicates variables with significant ( $p<0.05$ ) association with MRB-QoL domains; bold values denote  $aR^2$ .

**Abbreviations:**  $aR^2$ , adjusted regression coefficient; CCI, Charlson Comorbidity Index; CI, Confidence Interval; DBI, Drug Burden Index; MRCI, Medication Regimen Complexity Index.

### Therapeutic Relationship (TR) Domain

The mean score on the TR domain was  $6.5\pm 2.93$ . In linear regression analyses, all variables were significantly associated with TR domain scores except for MRCI ( $p=0.61$ ) (Table 2). In multivariable regression analysis, there was a significant association between age and TR domain (Table 3). Medication-related factors (ie, DBI,

MRCI, and number of medications) accounted for 4% of the variance in TR score. After adding medical condition-related factors (ie, CCI and number of medical conditions) and age, the total variance explained by the three factors increased to 19%, with age ( $\beta=0.08$ ) being the only variable significantly associated with TR outcome (Table 4).

**Table 4** Influence of Demographic and Clinical Characteristics on MRB-QoL (N=367)

Variables	Model I			Model II			Model III		
	$\beta$ (95% CI)			$\beta$ (95% CI)			$\beta$ (95% CI)		
<b>Routine and Regimen Complexity (RRC)</b>									
DBI	-2.69*	-4.34	-1.05	-1.72	-3.51	0.06	-1.23	-2.79	0.33
MRCI	0.01	-0.23	0.24	-0.07	-0.32	0.19	-0.20	-0.43	0.02
Number of medications	-0.76*	-0.23	0.24	-0.59	-1.27	0.09	-0.42	-1.01	0.18
Number of medical conditions				-0.73	-2.04	0.58	-0.15	-1.29	1.00
CCI				0.95*	0.27	1.63	-0.44	-1.11	0.23
Age							0.37*	0.29	0.45
aR <sup>2</sup>	<b>0.08</b>			<b>0.10</b>			<b>0.32</b>		
<b>Psychological Burden (PsyB)</b>									
DBI	-1.79*	-2.74	-0.85	-1.29*	-2.31	0.28	-1.15*	-2.14	-0.16
MRCI	-0.03	-0.16	0.11	-0.03	-0.17	0.12	-0.07	-0.21	0.07
Number of medications	-0.23	-0.51	0.05	0.10	-0.29	0.49	0.15	-0.22	0.53
Number of medical conditions				-1.05*	-1.79	-0.30	-0.88*	-1.61	-1.50
CCI				0.43*	0.04	0.82	0.02	-0.40	0.45
Age							0.11*	0.06	0.16
aR <sup>2</sup>	<b>0.07</b>			<b>0.10</b>			<b>0.16</b>		
<b>Functional and Role Limitation (FRL)</b>									
DBI	-2.55*	-3.63	-1.48	-2.01*	-3.19	-0.84	-1.79*	-2.91	-0.68
MRCI	0.11	-0.5	0.26	0.07	-0.10	0.23	0.01	-0.15	0.17
Number of medications	-0.47*	-0.79	-0.16	-0.39	-0.84	0.06	-0.31	-0.73	0.11
Number of medical conditions				-0.38	-1.24	0.48	-0.12	-0.94	0.69
CCI				0.53*	0.09	0.98	-0.01	-0.56	0.39
Age							0.16*	0.11	0.22
aR <sup>2</sup>	<b>0.10</b>			<b>0.12</b>			<b>0.21</b>		
<b>Therapeutic Relationship (TR)</b>									
DBI	-0.21	-0.68	0.25	0.11	-0.39	0.62	0.22	-0.26	0.69
MRCI	0.06	-0.01	0.12	0.03	-0.04	0.10	0.00	-0.06	0.07
Number of medications	-0.25*	-0.39	-0.11	-0.19	-0.38	0.01	-0.15	-0.33	0.03
Number of medical conditions				-0.26	-0.63	0.11	-0.14	-0.48	0.21
CCI				0.32*	0.13	0.51	0.03	-0.18	0.23
Age							0.08*	0.05	0.10
aR <sup>2</sup>	<b>0.04</b>			<b>0.08</b>			<b>0.19</b>		
<b>Social Burden (SB)</b>									
DBI	-1.06*	-1.74	-0.38	-0.56	-1.29	0.17	-0.39	-1.05	0.27
MRCI	0.06	-0.04	0.15	0.02	-0.08	0.13	-0.03	-0.12	0.07
Number of medications	-0.19*	-0.39	0.00	-0.09	-0.37	0.19	-0.03	-0.28	0.22
Number of medical conditions				-0.43	-0.96	0.11	-0.22	-0.70	0.27
CCI				0.48*	0.20	0.76	-0.02	-0.30	0.26
Age							0.13*	0.09	0.17
aR <sup>2</sup>	<b>0.04</b>			<b>0.08</b>			<b>0.25</b>		

**Notes:** Model I: Medication-related factors (number of medications, MRCI, DBI); Model II: adjusted for disease burden factors (CCI, number of medical conditions); Model III: adjusted for demographic factor (age);  $R^2$ , regression coefficient;  $aR^2$ , adjusted  $R^2$  (ie, the proportion of variance in the MRB-QoL domains explained by independent variables included in the regression models adjusted by the rest of the covariates); bold values denote  $aR^2$ ;  $\beta$ , regression coefficients (the change in the MRB-QoL domain in relation to the independent variables in the model adjusted by the rest of the covariates). \*Indicates variables with significant ( $p < 0.05$ ) association with MRB-QoL domains.

**Abbreviations:** CCI, Charlson Comorbidity Index; CI, confidence Interval; DBI, Drug Burden Index; MRB-QoL, Medication-Related Burden Quality of Life; MRCI, Medication Regimen Complexity Index.

### Social Burden (SB) Domain

The mean score on the SB domain was  $9.9 \pm 4.25$ . In linear regression analyses, all variables were significantly associated with SB scores except for MRCI ( $p=0.74$ ) (Table 2). The association was stronger for DBI, CCI, and number of medical conditions. For every unit increase in DBI and number of medical conditions, the SB score decreased by 1.02 ( $p<0.01$ ) and 0.44 ( $p<0.01$ ), respectively. In multivariable regression analyses, there was a significant association between age and the SB domain (Table 3). Medication-related factors (ie, DBI, MRCI, and number of medications) accounted for 4% of the variance in the SB domain score. The total variance in SB domain scores explained by all factors was 25%. Age ( $\beta=0.13$ ) was the only variable to significantly contribute to SB outcome (Table 4).

## Discussion

This was the first study to explore factors associated with the MRB-QoL outcome measure. The present study showed that DBI was the dominant medication-related factor associated with one or more domains of the MRB-QoL. After adjusting for covariates, an increase in DBI was associated with poorer Psychological Burden and Functional and Role Limitation, but not with Routine and Regimen Complexity, Therapeutic Relationship, or Social Burden domain scores. Although number of medicines was significantly associated with all domains of the MRB-QoL in univariate analyses, this association was not observed with any of the domains after adjusting for confounding factors. A further analysis by splitting the number of medications, with 5 as a cut-off point for polypharmacy, showed that polypharmacy was not associated with any of the MRB-QoL domains. Similarly, the MRCI was not significantly associated with any of the MRB-QoL domains except for Psychological Burden (in univariate analysis). The lack of association may be due to the lower complexity of the medication regimen, as observed in the calculated MRCI, with a median of 9.

To the best of our knowledge, no single study has evaluated medicine-specific measure(s) of quality of life in relation to DBI and complexity of the medication regimen to enable a comparison with our findings. Previous cross-sectional and longitudinal studies which used measures of HRQoL developed based on disease models reported significant associations between higher DBI and poorer physical functioning.<sup>14,15,17,25</sup> Similarly,

consistent with our findings, in a previous study, neither MRCI nor polypharmacy was associated with poorer HRQoL outcomes.<sup>13</sup> However, previous studies<sup>12,13</sup> evaluating the association between MRCI, polypharmacy, and HRQoL used a non-medicine-specific HRQoL measure, which may not be sensitive enough to capture changes in quality of life pertaining to polypharmacy or complexity of the medication regimen. It is noteworthy that the findings of our study also may not reflect the complete picture of the impact of polypharmacy or complexity of the medication regimen on the patient's quality of life. This may, in part, be due to the fact that the study participants were well-functioning community-dwelling adults with less complex medication regimens, as reflected in the MRCI scores. In addition, there was no access to data to determine evidence regarding the clinical inappropriateness of polypharmacy in the study population. These limitations call for further investigations into the impact of polypharmacy and complexity of medication regimens on quality of life in longitudinal studies and in patients with more complex medication regimens.

In this study, it was found that both CCI and number of medical conditions (as a continuous data) were significantly associated with all subscales of the MRB-QoL (in univariate analysis). However, after adjusting for age and medication-related factors, CCI was not significantly associated with all subscales of the MRB-QoL, whereas the number of medical conditions was associated only with the Psychological Burden domain. The impact of concurrent multiple chronic conditions on poorer HRQoL outcome is well established, with evidence gained from research using non-MRB-QoL measures.<sup>26</sup> In our study, the lack of association between the number of medical conditions and other domains of the MRB-QoL, such as Functional and Role Limitation, could be explained by the lower severity of disease, as participants were well-functioning community-dwelling adults. However, this study did not explore detailed information regarding the types of medical condition that were significantly associated with poorer psychological well-being. It may be important to investigate whether the association between the number and types of medical conditions and MRB-QoL is driven by the number of medications prescribed for a condition or by other factors.

Another finding in our study was that age was significantly associated with the scores on all MRB-QoL domains. The multivariable analyses results showed that medication-related quality of life tends to increase with increasing age.

While this could be due to a range of reasons, such as being on less complex medication regimens which can be easily managed by patients, participants were well-functioning community-dwelling adults and had low disease complexity; therefore, the overall impact of the disease on their health and well-being may be minimal. Despite this, the direction of the association between age and MRB-QoL domains needs further investigation. Contrary to our findings, an increase in age was associated with a decrease in HRQoL outcomes in a previous study evaluating the impact of chronic disease on HRQoL.<sup>27</sup>

The key strength of this study is the use of a validated medicine-specific measure of medication burden on quality of life. Our findings provide preliminary evidence regarding factors associated with MRB-QoL and highlight the importance of further exploring potential factors affecting medication-related quality of life outcomes in patients with multiple morbidities and multiple medications. This may help clinicians to tailor pharmacotherapeutic interventions and other management strategies to prevent or minimize factors contributing to poorer medication-related quality of life outcomes. Despite this, our study is not without some limitations. Associations between MRB-QoL and sociodemographic factors such as income level, and education/health literacy were not evaluated in this study. Moreover, owing to the cross-sectional nature of the data, it was not possible to infer causal relationships between poorer MRB-QoL outcomes and explanatory variables. Data were obtained from the MRB-QoL validation survey of well-functioning community-dwelling adults and, thus, results may be different for hospitalized patients and for patients with severe conditions or on clinically inappropriate polypharmacy. Furthermore, there may be a possibility of information bias owing to the self-reported nature of data on medication and medical conditions, which we did not confirm through reviewing medical records and medication charts. Although we have included potential factors that may influence medication-related quality of life outcomes, the models explained only 16–32% of the variability in MRB-QoL outcomes. This could be due to the cross-sectional nature of the data or there could be other unexplored factors potentially explaining the remaining variability in MRB-QoL outcomes. Moreover, the types and severity of medical conditions, and the clinical appropriateness of medications were not evaluated, and this may have affected the association between explanatory variables and MRB-QoL domains. Future investigations could therefore include

exploring the medication-related burden in different populations, such as patients recruited from hospitals and nursing homes, and those with different medical conditions, more complex medication regimens, and problematic polypharmacy.

## Conclusion

The findings of this study provide preliminary evidence on potential factors affecting medication-related quality of life outcomes. DBI was the dominant medication-related factor, which was significantly associated with poorer scores on the Psychological Burden and Functional and Role Limitation domains of the MRB-QoL. An increase in the number of medical conditions was associated with poorer psychological well-being. Neither polypharmacy nor MRCI was associated with any of the MRB-QoL domains. Future longitudinal studies along with further psychometric testing of the MRB-QoL measure are warranted to better understand predictors of medication-related quality of life outcomes.

## Ethical Approval

Ethical approval was obtained from the Human Ethics Committee, the University of Sydney (project number 2016/654). Prior to completion of the survey, all participants received a participant information sheet (PIS) and consent form (CF) containing detailed information about the study to help them make an informed decision. As approved by the ethics committee, informed consent was conferred through the return of completed questionnaires. The study was conducted in accordance with the Declaration of Helsinki.

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## Disclosure

The authors declare no competing interest in this work.

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