

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

The Association Between Multimorbidity and Health-Related Quality of Life Among Clients Attending Chronic Outpatient Medical Care in Bahir Dar, Northwest Ethiopia: The Application of Partial Proportional Odds Model

Fantu Abebe Eyowas (≤ fantuabebe@gmail.com) Bahir Dar University
Marguerite Schneider University of Cape Town
Shitaye Alemu University of Gondar
Sanghamitra Pati ICMR-regional medical research center
Fentie Ambaw Getahun Bahir Dar University

Research Article

Keywords: multimorbidity, quality of life, proportional odds, partial proportional odds model

Posted Date: November 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1089109/v1

License: (c) This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Abstract

Background

Multimorbidity, the presence of two or more chronic non-communicable diseases (NCDs) in a given person affects all aspects of individuals' lives. Poor quality of life (QoL) is one of the major consequences of living with multimorbidity. Although healthcare aims to support multimorbid individuals to achieve better quality of life, little is known about the effect of multimorbidity on quality of life of patients attending chronic outpatient medical care in Ethiopia.

Objectives

This study aimed to determine the association between multimorbidity and quality of life among clients attending chronic outpatient medical care in Bahir Dar city, Northwest Ethiopia.

Methods

A multi-centered facility-based study was conducted among 1440 participants aged 40+ years attending chronic outpatient medical care. Two complementary methods (interview and review of medical records) were employed to collect data on sociodemographic characteristics and presence of chronic diseases. We used the short form (SF-12 V2) instrument to measure quality of life. The data were analyzed by STATA V.16 and multivariate partial proportional odds model was fitted to identify covariates associated with quality of life, adjusting for relevant confounding factors. Statistical significance was considered at p-value <0.05.

Results

Multimorbidity was identified in 54.8% (95% CI=52.2%-57.4%) of the sample. A significant proportion (33.5%) of the study participants had poor quality of life and one fourth (25.8%) of them had moderate quality of life. Advanced age and living with multimorbidity were associated with poor quality of life. Conversely, being female, strong social support, high socioeconomic status, and adequate functioning and satisfaction with care were the variables positively associated with higher categories of quality of life.

Conclusion

The magnitude of multimorbidity in this study was high and individuals living with multimorbidity had a relatively poor quality of life than those without multimorbidity. Care of people with chronic multiple conditions may need to be oriented to the realities in multimorbidity burden and its implication on quality of life. Interventions targeting modifiable associated factors and studies exploring the longitudinal effect of multimorbidity on quality of life are needed.

Background

The increasing demographic and social change with ageing populations are leading to rapid epidemiological transitions including the rise of chronic non-communicable diseases (NCDs) and multimorbidity(1).

Multimorbidity refers to the presence of two or more coexisting long-term conditions, being related or not in a person (2). Despite the inconsistency in the methodologies employed to define and measure multimorbidity(3), evidence has shown that the burden of multimorbidity is growing globally (4, 5). It is projected that the number of people affected by multimorbidity is expected to double by 2035, and the majority of those who would survive beyond 65 years will have four or more chronic conditions(6, 7).

Advanced age (4, 8-11), socioeconomic deprivation (11), obesity(12), female sex (13, 14) and psychosocial factors such as social network and locus of control (15, 16) were the most common factors associated with multimorbidity in the global literature.

Multimorbidity affects all aspects of patients' lives; Poor quality of life (QoL) along with disability, functional decline and high health care costs are major consequences of living with multimorbidity(17, 18). The effect of multimorbidity on QoL was reported to be profound among the middle-aged, elderly, women and individuals with comorbid mental illnesses (13).

Living with multimorbidity is beyond the sum of individual chronic conditions (19). The specific disease clusters that an individual is living with would have a different effect on their physical and psychological functioning (20). For instance, the health-related QoL has always been lower among people living with multimorbidity compared to those without multimorbidity (21).

Lifelong presence of multimorbidity is also posing significant challenge for the health system (22). Individuals living with different types and combinations of NCDs may have different needs and priorities (23). Nevertheless, too little attention is paid to what matters to people living with multiple health problems (24, 25).

Moreover, the current model of care and guidelines being developed at a time when single disease frameworks were predominant tend to focus on diseases in isolation rather than the needs and circumstances of the person with complexity of the care needs as a whole (26, 27). As a result, people living with multiple conditions will get in contact with multiple health professionals which may not have proper communication and adequate data flow across the healthcare system, eventually leading to a fragmented, uncoordinated and siloed patient management (2, 28). Further, the rapid emergence of infections such as COVID-19 fuels the complexity and posing a huge burden to the health systems and worsening outcomes of patients with preexisting chronic diseases and multimorbidity (29, 30).

Several valuable studies investigated the relationship between QoL and multimorbidity (31, 32). However, most of them were conducted in high-income countries and the tools employed to measure QoL among people living with multimorbidity have not been consistent(33). Some studies in high-income countries used Euro QoL (EQ-5D-5I)(34, 35), while others used either WHOQOL brief(33) or SF-36 (33, 36) or SF-12

tools (33, 37-39). Although the usability of these tools has been widespread, the acceptability of the short form (SF-12) version is universal to study health related quality of life in the context of multimorbidity research(40).

The observed variations in the existing literature were not limited to only the tools to measure QoL, but also the methods of analyses of these data have hugely been different(41). The way the data have been generated is particularly important for analyzing quality of life assessments scores (42). Health related QoL is often measured by Likert-type scales and the scores are treated as if they were continuous and normally distributed, which often is not the case(43). Scholars in the field reported that analyzing ordinal data as if they were a metric one can systematically lead to distorted effect-size estimates, inflated errors rates and inaccurate parameter estimates (44, 45).

Neither do the methods used for binary data are adequate to fully take account of the properties of ordered outcomes such as QoL(41, 46). Hence, a more sensitive and comprehensive model is required. Evidence suggested that the ordinal regression models are superior to the methods commonly used to analyze data with ordered nature(47, 48). The ordinal models provide better theoretical interpretation and numerical inference than the metric models for ordered outcomes(49, 50).

However, the ordinal regression model provides unbiased estimates when the data meet the proportional odds assumption(46, 49). The PPO assumption implies that all observations have a common variance on the underlying continuum, and the coefficients that describe the relationship between, say, the lowest versus all higher categories of the response variable are the same except in the cut-off points(42, 48, 51)

However, it is often difficult to find data for which a proportional odds model is a plausible description, and evidence proclaims that the assumptions of the ordered logit (proportional odds) model are frequently violated(47). When the given data violates the parallel regression assumption, a more realistic approach, the partial proportional odds (PPO) model would be suitable(47). This model is robust to reveal unobserved heterogeneity in the group and identify correlates contributing to negative health outcomes, including impaired QoL(41, 46). The primary reason for the formulation of the partial proportional odds models is to relax the stringent assumption of constant odds ratio over all the cut-points for a given covariate(48).

Supporting people living with long-term conditions to maintain a good quality of life is one of the key challenges facing the healthcare and social care systems today (18). Studies suggested that the management of patients with multimorbidity to take into account the impact of multimorbidity on a person's quality of life and their priorities (52, 53). However, nothing is known about the effect of multimorbidity on health-related QoL in the country. If health systems are to meet the needs and priorities of individuals living with multimorbidity, we need to adequately measure the magnitude and impact of multimorbidity on QoL among the chronic patient population.

The present study aimed to understand the association between multimorbidity and QoL among individuals attending chronic outpatient medical care in Bahir Dar, Northwest Ethiopia.

Methods

This facility-based study was conducted in eight health facilities providing chronic NCDs care in Bahir Dar City, Ethiopia. The detail of the methods employed in this study has been published elsewhere (54).

Design

This multi-center facility-based cross-sectional study conducted in public and private health facilities rendering health services in Bahir Dar City, Ethiopia. The city is the capital of the Amhara regional state-the second populous region in the country, where about 31 million people are living(55).

Study setting and population

This study was conducted in five hospitals (three public and two private) and three private higher/specialty clinics in the city. These facilities also serve as referral center for primary care facilities surrounding the regional capital. Chronic NCDs care and management is presumed to be provided in a relatively uniform fashion using the national NCDs treatment guideline (56). However, the nature of patients vising these facilities may vary and there remains a concern on quality and affordability NCDs care in public hospitals and private health facilities, respectively.

Only facilities which were providing chronic NCDs care by medical doctors (general practitioners or specialist physicians) for at least a duration of one year prior to the data collection period were considered. Older adults (40 years or more) diagnosed with at least one NCD and were on chronic diseases follow up care for at least six months at the time of the study period were recruited for the study. However, pregnant women and individuals who are too ill to be interviewed and admitted patients were excluded.

Sample size

Key issues considered to estimate the sample size required were the nature of the dependent and predictor variables and the anticipated data analysis techniques. The input values: a (type I error=0.05), power (1-b=90), confidence level (95%) and the estimated non-response and attrition during follow-up (20%) remain constant. The authors found the general linear multivariate model with Gaussian errors (GLIMMPSE) sample size and power calculator (32-34) the method yielding the maximum sample size compared to other techniques. Based on the given assumptions and the approach we used, the sample size became 600. As the nature of participants is likely to be different by the type of facility (public or private) they receive care, we employed stratification to ensure fair representation in the sample for important sub-groups. Hence, a design effect of 2 was considered to avoid the possible loss of sample during stratification. Adding 20% to the possible loss to follow-up (considering the upcoming longitudinal study) and nonresponse, the sample size needed was calculated to be 1440.

Sampling Technique

A two-stage clustered stratified random sampling method was employed for recruiting eight eligible facilities and a corresponding number of participants. The sample size from each facility was determined based on the notion of probability proportional to size (PPS) using the pool of chronic NCD patients (³ 40yrs) registered for follow-up over the year preceding our assessment (January - December 2020) in each participating facility. Health facilities and eligible clients were randomly selected for the study.

Definition and measurement of Dependent Variable (HRQoL)

HRQoL (stated as QoL in this study) is defined as individuals' perception of their position in life in the context of physical, psychological and social functioning and well-being (57). QoL was measured using interviewer-administered short form (SF-12 V2) assessment tool (58, 59), which is derived from the SF-36 QoL assessment tool (40).

The tool was extensively validated and widely used generic tool for measuring QoL in multimorbidity across different contexts (39, 60). The SF-12 measures eight health aspects, namely physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (psychological distress and psychological well-being) (MH). Two summary measures are derived from the SF-12: physical health (Physical Component Summary-PCS) and mental health (Mental Component Summary -MCS). However, owing to the possibility of correlation (lack of uni-dimensionality) between the PCS and MCS scores, some studies criticized the use of these scoring algorithms and recommended raw sum scores instead(40, 45). The use of a single raw sum score enables a consistent assessment of the impact of multimorbidity and how this varies across a given population(61). Thus, we applied this approach for analyzing the QoL data.

First, we reverse coded the scores for items 1, 9 and 10 and computed the raw total. The overall scores were scaled from 0 to 100, with 0 representing worst health (62). Although popularly used in previous studies, the notion of fitting linear regression models to summarize categorical data such as the QoL data is refutable(42, 45). The linear regression models may potentially lose important variability in the data particularly when the QoL data is collected by Liker-type scales such as the SF-12 tool(41, 46). Recent advances in field recommended interpretation of QoL as a categorical (group continuous) variable than as a metric variable(42). Studies suggest that ordinal regression models (OLR) are superior to other method for analyzing ordinal data, including health-related QoL data(42, 43). Hence, we ranked the scaled QoL scores into three ordered and non-overlapping categories as poor QoL (a scaled value <75), moderate QoL (scaled value from 75-89.9) and high QoL (scaled value from 90-100) (46) and fitted into the OLR and partial proportional odds (PPO) models.

Measurement of independent variables

Independent variables including socio-demographic characteristics [age, gender, education, marital status, residence and occupation] were assessed using validated tools. Whereas, data to calculate body mass index (BMI) and waist to hip circumference were directly measured from patients according to the approaches described in our study protocol published elsewhere(54).

Social networking and support system was assessed through face-to-face interview using pre-tested and standardized tools (Oslo Scale) (63). A scale ranging from 3–8 was interpreted as poor social support, 9–11 moderate social support and 12–14 strong social support) (63).

Wealth Index at a household level was generated from a combination of material assets and housing characteristics (64). The Wealth index was scored using principal component analysis (PCA) technique. The score was classified into quintiles, for urban and rural residents separately, while quintile 1 represents the poorest and quintile 5 the wealthiest (65). It was collapsed into three classes as low, middle and high income.

Multimorbidity was operationalized as the co-occurrence of two or more of the chronic NCDs, including hypertension, diabetes, heart diseases (heart failure, angina and heart attack), stroke, bronchial asthma, chronic obstructive pulmonary diseases (COPD), depression, cancer, musculoskeletal disorders (arthritis, chronic back pain and osteoporosis), thyroid disorders (hyperthyroidism and multinodular goiter), chronic kidney disease, gastrointestinal disorders (chronic liver, gall bladder and gastric diseases) and Parkinson's disease (PD). The list of NCDs identified for the study was determined based on a review study(66) and preliminary and pilot studies conducted prior to the main study. Information on these chronic conditions was obtained from interview and review medical records using standardized tools (54).

As to functional capacity, patients were asked to globally rate their overall functional status (as excellent, good or poor/limited capacity).

Data Collection Tools and Procedures

As mentioned above, the data were collected mainly from different sources: interview and review of medical records. The questionnaire to collect the data was translated to Amharic (local language) and pilot tested for cross-cultural adaptability based on standard protocols (67, 68). The data were collected by the Kobo Toolbox software(69). Patients were interviewed and assessed following consultation periods. Physicians and nurses working in the chronic care unit were involved in the data collection process.

To ensure data quality, data collectors and supervisors were provided with a two-days training detailing the study, including obtaining written consent, conducting face-to-face interview, performing physical measurement, medical record review and navigating through the questionnaires in the Kobo toolbox platform preloaded into their smart phones. The data collection process was monitored by trained supervisors, and the principal investigator. The data sent to the Kobo toolbox server were checked daily for completeness, accuracy and clarity.

Data Analysis

The data from the Kobo toolbox server were downloaded into excel spreadsheet and exported to SPSS V. 21 for cleaning and the data were analyzed by STATA V. 16. Descriptive statistics were computed to describe the sociodemographic characteristics of participants. The magnitude of individual chronic conditions and multimorbidity was determined by combining data from different sources, including patient interview and medical record review.

In addition, the proportion of individuals falling into each of the QoL category was calculated. QoL as an ordered outcome was categorized as low, moderate and high, and coded as 0, 1 and 2, respectively while fitting into the ordinal logistic regression model. The association between each explanatory variable and QoL was assessed separately and model fitness was checked using the proportional odds (test for parallel regression) assumption(47). The proportional odds (PO) assumption is said to be satisfied when we fail to reject the null hypothesis (a p-value of >0.05 in the Brant test) in the ordinal logistic regression model (47, 48).

For variables which fail to satisfy the PO assumptions, the OLR model cannot fit the data well (48). Rather, the partial proportional odds (PPO) model would be appropriate(41, 46). The partial proportional odds (PPO) model bridge the gap between ordered and non-ordered modeling frameworks (49, 70). While the ordinal logistic regression model is restrictive and assumes that the effect of independent variables remain the same (fixed) for all levels of the dependent variables, the PPO allows the independent variables to take into account the individual differences in their effect on the dependent variables(48, 71). Compared to the OLR model, the PPO is performed well in studies that compared different analytical models fitted for QoL data(42, 46). Hence, we fitted the PPO (gologit2, autofit Irforce and gologit2, autofit Irforce gamma commands) model for determining covariates associated with QoL and to clearly identify the variables which violates the assumptions.

The independent variables fitted into the PPO model included residence, sex, age, marital status education, education, BMI, social support, SES, multimorbidity, self-rated functional capacity and satisfaction with care. Independent variables having more than two categories were collapsed into two categories while fitting the PPO model(47). The association between QoL and independent variables was assessed by fitting univariate and multivariate odds ratio (OR) with 95% confidence intervals and p-values are reported for each of the independent variable analyzed. Variable having a p-vale £0.2 were fitted into multivariable PPO models to predict the adjusted effect of the independent variables on QoL. Before running the multivariable analysis, multi-collinearity between independent variables was checked using the Variance Inflation Factor (VIF) and variables were not strongly correlated (the highest value was 1.05). To make the interpretation more straightforward, we expressed the effects in terms of odds ratio than as regression coefficients(46). In all cases, a p-value £ 0.05 was taken as a statistically significant relationship.

Results

Characteristics of the Study Participants

Complete data were obtained from 1432 individuals giving rise to a response rate of 99.4%. Females constitute a slightly higher (51%) percentage in terms of sex distribution. The mean (±SD) age of the participants was 56.4 (±11.8) years. Individuals aged 45-54 years and 55-64 years accounted almost equally (27.9%) for the age distribution and those aged 65+ had a 26.9% share from the total sample (Table 1).

The majority of participants (75.5%) were married at the time of data collection. Looking into the education level of the respondents, a little more than half (54.5%) of them did not attend any formal education. Urban residents accounted the largest (70.3%) proportion, and housewives (23%) and employed individuals (22.9%) represent the largest proportion in the occupation category. The highest percentage (37.4%) of the participants had low SES (Table 1).

Table 1: Socio-demographic characteristics of study participants attending chronic outpatient NCDs care in Bahir Dar, Ethiopia (N=1432)

Variables	Frequency	Percentage
Age group £44Yrs	247	17.3
45-54Yrs	399	27.9
55-64Yrs	400	27.9
65+Yrs	386	26.9
Sex Male	702	49.0
Female	730	51.0
Marital status Currently married	1081	75.5
Single*	351	24.5
Education No formal education	780	54.5
Primary education (Grade 1-8)	166	11.6
Secondary (9-12)	171	11.9
College level and above	315	22.0
Residence Urban	1007	70.3
Rural	425	29.7
Occupation Housewife	329	23.0
Employed (government and private)	328	22.9
Farmer	288	20.1
Trader	207	14.5
Retired	141	9.8
Unemployed	139	9.7
Wealth Index (SES) Poorest	269	18.8
Poorer	334	23.3
Middle	267	18.6
Rich	252	17.6
Richest	310	21.6

*Includes never married, divorced, widowed and separated

Lifestyle and Psychosocial Characteristics

The highest percentage (53.3%) of participants had normal body mass index (BMI) (Figure 1). The mean of social support scale was 10.2 and standard deviation (SD) of \pm 2.17 scores. Just half (50.7%) of the participants reported that they have moderate social support, and about one third (28%) reported strong social support, while the remaining 21% reported that they have a poor social support.

Magnitude of NCDs and number of chronic NCDs identified per person

The magnitude of each of the chronic conditions considered in this study is shown in figure 2. The number of NCDs identified per person ranged from one to four (mean=1.74, SD=0.78). Hypertension was the most frequently reported NCD (63.5%), followed by diabetes (42.5%) and heart diseases (25.6%).

Magnitude of Multimorbidity

More than half 54.8% (CI=52.2%, 57.4%) of the study participants had multimorbidity, from which, 39.6% had two chronic NCDs and 15.2% of them had three or more chronic NCDs.

The most prevalent NCDs have highly contributed for shaping the patterns of multimorbidity in this study. For example, hypertension was co-existed with diabetes and heart diseases in 38.2% and 19.0% of the participants, respectively. Similarly, co-occurrence of diabetes was observed among individual with heart diseases, depression and other types of reported chronic conditions. Hypertension remained the most frequently reported NCD (87.2%) among individuals living with three or more NCDs in our study. Diabetes was reported by 51% of those who had three or more chronic NCDs and heart diseases were reported by 39% of the participants from this group (Table 2).

Table 2: Distribution of individual NCDs and their pairwise and triples or quadruples combination, among people attending chronic outpatient NCD care in Bahir Dar, Ethiopia (N=1432)

Single morbidity		Common pairs of NCDS		Common Triples of NCDs		
Chronic NCD	Frequency(%)	Combination	Frequency(%)	Combination	Frequency(%)	
Hypertension alone	245 (37.9)	Hypertension +Diabetes	217 (38.2)	Hypertension +Diabetes+ heart diseases	19 (8.7)	
Diabetes alone	225 (34.8)	Hypertension + Heart diseases	108 (19.0)	Hypertension +Diabetes + depression	18 (8.3)	
Heart diseases alone	120 (18.5)	Hypertension + stroke	38 (6.7)	Hypertension +Diabetes + other NCDs	49 (22.5)	
All other forms of single NCDs ^a	57 (8.8)	Hypertension +Musculoskeletal diseases	23 (4.0)	Hypertension +heart diseases + other NCDs	43 (19.7)	
		Hypertension + Asthma	21 (3.7)	Hypertension + Diabetes + heart diseases + other NCDs	12 (5.5)	
		Hypertension + Chronic Renal diseases	21 (3.7)	Hypertension + Diabetes + two other NCDs	13 (6.0)	
		Hypertension + Depression	18 (3.2)	Hypertension + two or other NCDs	36 (16.5)	
		Hypertension + other chronic diseases	25 (4.4)	Diabetes + two or more other NCDs	13 (6.0)	
		Diabetes + Depression	8 (1.4)	Heart diseases + two or more other NCDs	11 (5.0)	
		Diabetes + heart disease	6 (1.0)	Triple or quadruple of all other NCDs	4 (1.8)	
		Diabetes + other chronic NCDs	25 (4.4)			
		Heart disease +Depression	16 (2.8)			
		Heart diseases + other chronic Page 12	27 (4.8)			

diseases	
Comorbidity of other NCDs	14 (2.5)

^a Includes asthma, COPD, stroke, cancer and depression

A significant proportion (33.5%) of the study participants had poor quality of life and about one fourth of them had moderate QoL (Figure 1).

Individuals living with multimorbidity had a relatively poor QoL than those people living without multimorbidity (62% vs.38%). Similarly, highest proportion of individuals with severe functional limitation had altered QoL than those without severe limitation (Figure 5).

Table 3 shows the output of univariate ordinal logistic regression analysis. Except for sex, residence, marital status and education level, all the explanatory variables were significantly associated with QoL. Looking at the Brant test of significance, most of the explanatory variables satisfied the proportional odds assumption. However, five variables (sex, social network, SES, self-rated functional status and satisfaction with care) violated the assumption of parallel lines (p-value £0.05), warranting the application of multivariate partial proportional odds model (Table 3).

Table 3: Univariate ordinal logistic regression analysis and estimates for proportional odds assumption

Variables	QoL cat	QoL category			Brant
	Poor QoL	Moderate QoL	High QoL		test
Residence Urban	272	273	462	Base	
Rural	208	97	120	<0.474	
Sex Male	207	174	321	Base	0.037**
Female	273	196	262	0.200	
Age Mean	60.0	56.0	53.6	<0.001*	0.377
SD	12.61	11.30	10.62		
Education Below primary	360	191	229	0.557	
Primary and above	120	179	353	base	
Marital status Married	312	284	486	base	
Single	168	87	96	<0.648	
BMI £24.99	250	209	304	Base	0.665
³ 25	115	41	55	<0.023*	
SES Low	234	128	174	Base	<0.365
Middle or high	133	109	163	0.003*	
Social support scale Mean	9.3	10.6	10.7	<0.001*	<0.001**
SD	2.17	1.70	2.19		
Overall functioning Limited/weak capacity	258	29	5	base	<0.001**
Strong capacity	222	341	577	<0.001*	
Care satisfaction not satisfied	108	43	32	base	<0.001**
Satisfied	372	327	550	0.019*	
Multimorbidity No	182	170	295	base	0.016**
Yes	298	200	287	<0.001*	

*Statistically significant at p-value 0.05, **variables that violated the PPO assumptions

Multivariable partial proportional odds analysis

As stated above, the nature of the independent variables necessitates fitting of the partial proportional odds PPO model. The partial PPO model allows variables that meet the assumption to be modeled with the proportional odds assumption, whilst allowing others to have odds ratios that vary for the different categories that are compared. Only the variables with a p-value £0.2 in the univariate ordinal logistic regression analysis were fitted into the multivariate glogit2 (partial proportional odds) model.

Fitting the partial proportional odds assumption requires that the independent variables to have only two categories. Accordingly, except for age and social support score, we coded independent variables as a binary (0,1) response category, where higher values were coded as "1" and low values were given "0" and treated as a base category. Therefore, sex was coded as male (0) and female (1), SES as low (0) and middle or high (1), BMI as £24.99 (0) and ³25 (1), multimorbidity as no (0) and yes (1), functioning as severe limitation (0) and no or mild limitation (1) and satisfaction as not satisfied (0) and satisfied (1). Whereas, age and social support scale were treated as continuous independent variables. The outputs from the glogit2 command, glogit2 auto-fit Irforce command and the glogit2 auto-fit Irforce gamma commands had no statistically significant difference when the autofit statistics was set to be 0.05.

However, owing to the possibility that the observed violations of assumptions might be due to chance, and that testing violation of assumptions cannot be supported with theories (49), a more stringent significance level such as changing the default autofit significance level from 0.05 to 0.01 was considered in the final model. Although this model has shown to constrained some of the variables to meet the PPO assumption, the global parallel-lines assumption for the final model was not met (Chi-square 21.8, p-value 0.005). Hence, we decided to present the result of the default glogit2 auto-fit Irforce command instead.

In this model, the Wald test of parallel-lines assumption for the final model was insignificant (Chisquare=4.80, p-value 0.187) indicating that the final model does not violate the proportional odds/parallel-lines assumption.

The outcome variable, QoL (Y) is categorized into three (poor, moderate and high), so the model produced two panels. The first panel contrasts category 1 (poor QoL) with category 2 (moderate QoL) and 3 (high QoL) and the second panel contrasts category 1 and 2 with category 3. An odds ratio value greater than 1 (positive coefficient) on the explanatory variable indicates that it is more likely that the respondent will be in a higher category of Y than the current one (increasing in the explanatory variable led to higher levels of QoL); whereas, an odds value below 1 (negative coefficient) indicates the likelihood of being in the current or a lower category.

As sex, SES, social support scale, self-rated functioning and satisfaction with care violated the proportional odds assumption, the odds ratios were allowed to vary (AOR1 \neq AOR2). AOR1 stands for panel one (low versus moderate or high QoL), while AOR2 refers to the second panel (low/ moderate versus high QoL). However, for the independent variables which met the parallel regression assumption (Brant test value ³0.05), the odds ratio would be the same (AOR1 = AOR2) for the two panels.

Looking into the final model, statistically significant differences were observed in terms of the effect of most of the explanatory variables on QoL, adjusting for all the covariates.

The model indicates that the odds of being in the combined categories of moderate and high QoL versus poor QoL was 1.27 times higher for females than males, given the other variables held constant [AOR1 = 1.32 (95% Cl: 1.04, 1.68)]. However, the odds of being in the combined categories of moderate and low versus high QoL was lower by a factor of 0.06 for females than males. It was not, however, statistically significant [AOR2 = 0.94(95% Cl: 0.75, 1.17)].

The odds of being in the combined categories of moderate and low QoL versus high QoL was 0.34 times lower for individuals having a higher SES than the poorest category [AOR2 = 0.66(95% CI: 0.53, 0.84)]. However, SES did not show a statistically significant effect on the low QoL versus the combined moderate and high QoL category [AOR1 = 0.92(95% CI: 0.72, 1.18)].

As regards to self-rated functional capacity, the odds of being in the highest QoL category versus the combined categories of moderate and low QoL was 1.5 times higher for individuals reported to have strong capacity than those people with limited capacity [AOR2 = 1.48(95% CI: 1.11, 1.98)]. Likewise, although statistically insignificant, the odds of being in the combined categories of moderate and high QoL versus low QoL was 1.09 times higher for individuals reported to have strong physical functional capacity than those people with limited capacity [AOR1 = 1.09(95% CI: 0.82, 1.47)].

For a unit increase in the social support scale, the odds of being in the higher categories of QoL versus lower categories was 1.43 times greater [AOR1 = 1.43(95% Cl: 1.35, 1.51)]. Similarly, the odds of being in the higher category of QoL vs the combined categories of moderate and low QoL was 1.22 times higher [AOR2 = 1.22(95% Cl: 1.15, 1.28)], given the other variables held constant.

Similarly, the odds of being in the higher QoL category versus the combined categories of moderate and low QoL was 2.46 times higher for individuals reported to have satisfaction with care [AOR2 = 2.46(95% Cl: 1.70, 3.56)]. Likewise, although statistically insignificant, the odds of being in the lower QoL category versus the combined categories of moderate and high QoL was lower by 17% for individuals reported to have satisfaction with care than those who were not satisfied with the care they received [AOR1 = 0.83(95% Cl: 0.58, 1.19)].

Meanwhile, the variables that did not violate the PPO assumption had a constant beta coefficient (AOR1 = AOR2) for each of the two QoL categories; hence a single odds ratio was reported. In this study, for every one-year increase in age of the participants, the odds of being in the lower QoL category was increased by a factor of 0.04 [AOR1= AOR2: 0. 96 (95% CI: 0.95, 0.97)].

Similarly, the odds of being in the higher categories of QoL was 0.32 times lower for individuals living with multimorbidity than those people without multimorbidity [AOR1 = AOR2: 0.68 (95% CI: 0.55, 0.83)]. However, BMI did not remain statistically significant in the multivariable model [AOR1 = AOR2: 0. 84 (95% CI: 0.67, 1.05)] (Table 4).

	Outcome variables (panels)						
Explanatory Variables	Panel One (1 Vs. 2 and 3)			Panel Two (1or 2 Vs 3)			
	AOR 1 (95%CI)	Coefficients constant (OR1=OR2)	P- value	AOR2(95%CI)	P- value		
Sex (Female vs. male[Ref])	1.27 (1.01, 1.60)		0.048	0.94(0.75, 1.17)	0.563		
SES (high vs. low [ref])	0.92(0.72, 1.18)		0.517	0.66(0.53, 0.84)	<0.001		
Self-rated functioning (Strong vs. weak [Ref])	1.09(0.82,1.47)		0.534	1.48(1.11, 1.98)	0.005		
Satisfaction (satisfied vs. not satisfied [Ref])	0.83(0.58,1.19)		0.323	2.46(1.70, 3.56)	<0.001		
Social support scale	1.43(1.35, 1.51)		<0.001	1.22(1.15, 1.28)	<0.001		
Multimorbidity (yes vs.no [Ref])		0.68(0.55, 0.83)	<0.001				
Age in years		0.96(0.95, 0.97)	<0.001				
BMI (³ 25 vs. <24.99 [Ref])		0.84(0.67, 1.05)	0.124				

Table 4: Multivariable partial proportional odds model showing the association between factors and QoL

Discussion

Understanding the effect of multimorbidity on health related quality of life (QoL) is one of the top research priorities in the existing literature(72, 73). A broad sample of health facilities where most of the people living with chronic NCDs receive their care and corresponding number of patients were randomly selected and enrolled to determine the magnitude of multimorbidity and its association with QoL in the study area. We employed a blend of methods (face-to-face interview and review of medical records) to better determine the presence of individual NCDs and their pairwise and triple combination among a broad sample of 1432 individuals (aged 40+) attending chronic medical care in hospitals and specialized health facilities in Bahir Dar city, Northwest Ethiopia.

The implication of our findings should be interpreted in light of the variations in the way QoL has been measured and analyzed globally. The authors used the very commonly used QoL measure, the SF-12V2 tool, however, the method of analysis we employed- the partial proportional odds (PPO) is relatively new

in the context of analyzing QoL data(74). The PPO model is said to be a robust QoL data analytic method compared to other method of analysis provided the nature of a given data warrants its use(41).

In this study, the authors found that multimorbidity is common, affecting majority (55%) of the individuals receiving outpatient medical care. The high burden of multimorbidity in the study area implies that individuals living with chronic conditions have already been facing the overwhelming consequences of multimorbidity.

It was found that a higher proportion (33.5%) of individuals living with chronic NCDs had poor QoL, of which 62% was implicated by presence of multimorbidity. Several studies have shown that multimorbidity is a key factor contributing for poor QoL (31, 32, 36). Although direct comparison may not be possible with most of the previous studies owing to methodological variations, it was observed that patients with multimorbidity had significantly poorer quality of life compared to patients without any comorbid chronic conditions. Studies which utilized the PPO model to analyze QoL data have also reported consistent results corroborating the negative association between multimorbidity and QoL(74). However, evidence shows not only the mere sum of individuals conditions, but also the nature of disease cluster matter quality of life, functionality and survival (58).

Consistent with previous studies(13, 17), people with advanced age were shown to have reduced QoL in our study. Advanced age is known to impair molecular and cellular functions that leads to a gradual decline in the physiological reserves and capacity of the individuals (75). The observed inverse relationship between advanced age and poor QoL may also be due to the mediated effect of multimorbidity as the probability of having multimorbidity was higher among the middle-aged and elderly in our study. Although it is expected that people in old age often face poor quality of life due to physical disability, frailty and sensory impairment (22), earlier onset of multimorbidity and its effect on QoL was reported to be higher among young adults living in socioeconomically deprived areas(76).

The available literature on the associations between sex and QoL reported inconclusive results(76). In their review, Kanesaraja and colleagues (77) reported a negative association between female sex and poor QoL. However, the authors found females to have a higher levels QoL than males. This may be explained by the fact that females were relatively younger (mean age= 54.8 years) than males (mean age= 58.0 years) in our study. In addition, the variation in the type of diseases and their distribution between females and males might have contributed to the observed difference in the quality of life of individuals (58).

In agreement with other studies(78, 79), individuals in the wealthier quintile had better QoL than their poorest counterparts. Studies have also shown that economically deprived people struggle to cope with everyday life activities and have a lower quality of life compared with more affluent patients with multimorbidity (11). Further, multimorbidity was associated with a more significant reductions in QoL scores amongst participants living in the most deprived areas (76), signifying a coupling effect of poverty and multimorbidity on QoL. However, it is worth noting that the pathway of this relationship may not necessarily be unidirectional(80).

Medical care alone cannot adequately improve QoL(18). The presence of strong social support is helpful to improve patient's adaptation to life and their QoL(81). The authors found a positive and statistically significant association between perceived social support and QoL. However, some studies were inconsistent in reporting the effect of social support in modifying QoL among individuals living with multimorbidity(82-84).

Having multiple conditions increases the risk of disability and physical limitations(18, 85). The existing literature has shown that impaired functioning was negatively associated with QoL(86). Our study has also shown that individuals with limited functional capacity had poor quality of life. However, some caution needs to be taken in interpreting the results as the association between impaired functioning and QoL might be due to the negative effect of multimorbidity on functioning (18, 87). Furthermore, given functional capacity was assessed by self-rated single item global measure it our study, it may be important to consider this while comparing the results with other studies. Conversely, however, there is still lack of consensus on the pathway from chronic diseases to impaired physical functioning and the mechanisms whereby chronic multiple conditions are leading to disability or vice versa(87).

People living with multimorbidity are generally less satisfied with the care they receive(2). Ensuring satisfaction with care for people with multiple chronic health conditions is challenging because the notion of satisfaction is influenced by several actors, including caregivers, healthcare providers and the health system in general(18). In this study, it was observed that individuals satisfied with care were more likely to have higher odds of QoL. This is in congruent with previous findings substantiating that improving the quality of multimorbidity care would increase patient satisfaction and consequently improve the quality of their life(88). However, other literature shows no difference between satisfaction with care and improved QoL(28, 89).

Implication for healthcare and research

The main goal of health care for the people living multiple chronic conditions is to help them achieve better QoL(18, 90). Given that the magnitude of multimorbidity is huge and that it poses a profound effect on QoL in our study, the health system in context need to be oriented and guided these facts to adequately respond to individual patient needs. Care for people living with multimorbidity need to be based on the needs and circumstances of the person as a whole rather than the different conditions a person happens to have(89). The provision of patient-centered care in which all healthcare providers work together with patients to ensure coordination, consistency and continuity of care over time is essential (91). This will inter improve the wellbeing and survival of the people living with multimorbidity in the study area.

The evidence base on the association between multimorbidity and QoL is growing, albeit slowly. However, the methodologies employed to study multimorbidity are hugely inconsistent(3). Neither do the methods applied to investigate the effect of multimorbidity on QoL have been universally consistent(76). We are aware of the possible limitation of comparing our results with studies that employed different tools and methods of analysis of QoL data. Research is needed to furthering the application of ordinal regression

and PPO model for analyzing QoL data and to identify the covariates associated. Understanding the longitudinal effect of individual NCDs, multimorbidity and disease severity on QoL would help fill the substantial gaps in our knowledge in this regard. It is also imperative to study the way health systems are organized to manage patients with multimorbidity, and to explore the perspective and lived experiences of individuals living with multiple chronic conditions in the country.

Strength and Limitations of the study

Our study has the advantage of involving a broader range of health facilities rendering comprehensive care for the people living with chronic NCDs. Guided by a published study protocol, this study employed three complementary methods to define the presence of chronic NCDs accurately. The PPO model applied helped us to plausibly categorize the QoL data and identify covariates associated with QoL in a relatively efficient, reliable and valid way. However, the findings of this facility-based study may not exactly represent the underlying epidemiology of multimorbidity and the patterns of association between multimorbidity and QoL in the general population in Bahir Dar and beyond. It is also difficult to confirm that the observed association between the variables has a temporal relationship. Variables measured by Likert-type scales, in general, are subjected to bias. The lack of consistent methods to measure both multimorbidity and QoL globally makes our findings comparable to only some of the existing literature.

Conclusion And Recommendations

The magnitude of multimorbidity in this study was high. The high multimorbidity estimate observed in this study might be attributed to the fact that the study was conducted among health facilities where most of people living with chronic NCDs were attending care. Advanced age and living with multimorbidity were negatively associated with poor QoL. In contrast, female gender, high perceived social support, high SES, functioning and satisfaction with care were the variables associated with higher categories of QoL.

The literature on the relationship between multimorbidity and QoL is dominated by studies in high income countries. If health systems in LMICs are to meet the needs of the people with multimorbidity, it is essential to understand the full breadth of multimorbidity across the ages and its effect on individuals QoL, functioning and survival. Future studies may need to focus on understanding the epidemiology of multimorbidity and its effect on QoL in the population. Further studies (such as the one being conducted by the authors of this manuscript) are also needed to explore the longitudinal effect of multimorbidity on quality of life, functioning and survival, and to assess how health services are oriented and organized to meet the care needs of the people living multiple chronic conditions in the country. It is also imperative to replicate the methods which were employed to measure and analyze QoL data in this study. That would facilitate comparison and further development of the approaches.

Abbreviations

BMI Body Mass Index

QoL Quality of life

LIMCS Low-and middle-income countries

PO Proportional odds

PPO Partial proportional odds

NCD Non-communicable disease

SES Socio economic status

SF Short form

Declarations

Ethics approval and consent to participate in the study

As this is a part of an ongoing PhD study, permission to conducting the study has been obtained from the Institutional Review Board (IRB) of the college of medicine and health sciences, Bahir Dar University with a protocol number 003/2021. Study participants were enrolled after giving verbal consent to participate in the study. The adequacy of oral consent was approved by the IRB and the consent was documented on participants' information sheet. Permission was obtained from the health facilities involved in the study. Moreover, confidentiality of the data obtained from the study participants and medical records have been strictly maintained.

Patient consent for publication: Not applicable.

Availability of data and materials: all relevant data are included in the article and will also be published in relevant repositories accordingly.

Competing interests: None declared.

Funding Statement

Funding: This work was partially funded by Bahir Dar University [grant number: RCS/003/21]. No other funding support was obtained by any of the authors to pursue this study as yet.

Disclaimer: The funders had no roles in study design, fieldwork, data analysis, interpretation, and decision to publish the manuscript.

Author contribution

FAE, FAG, MS and SA conceived and designed this study. FAE, FAG, MS, SA and SP participated in the data analysis and interpretation of the findings. FAE drafted the manuscript and FAG, MS, SA and SP

contributed in revising the manuscript. All authors critically reviewed and approved the final manuscript for submission.

Acknowledgements

We thank Bahir Dar University for partially funding this study. We also thank Jhpiego-Ethiopia for the facilities we used to conduct this study. We would like to also thank data collectors, supervisors, facilities leaders and study participants for their support in making this study a reality.

References

- 1. WHO. World health statistics 2016: monitoring health for the SDGs, sustainable development goals2016.
- Mercer S, Salisbury C, Fortin M. ABC of multimorbidity First Edition. ed. UK: John Wiley & Sons, Ltd.; 2014.
- 3. Ho IS-S, Azcoaga-Lorenzo A, Akbari A, Black C, Davies J, Hodgins P, et al. Examining variation in the measurement of multimorbidity in research: a systematic review of 566 studies. The Lancet Public health. 2021;6: e587–97.
- 4. Xu X, Mishra GD, Jones M. Mapping the global research landscape and knowledge gaps on multimorbidity: a bibliometric study. Journal of global health. 2017;7(1):010414.
- Zemedikun DT, Gray LJ, Khunti K, Davies MJ, Dhalwani NN. Patterns of Multimorbidity in Middle-Aged and Older Adults: An Analysis of the UK Biobank Data. Mayo Clinic proceedings. 2018;93(7):857-66.
- 6. Calderon-Larranaga A, Vetrano DL, Ferrucci L, Mercer SW, Marengoni A, Onder G, et al. Multimorbidity and functional impairment: bidirectional interplay, synergistic effects and common pathways. Journal of internal medicine. 2018.
- KINGSTON A, ROBINSON L, BOOTH H, KNAPP M, JAGGER C. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. Age and ageing. 2018.
- 8. Mounce LTA, Campbell JL, Henley WE, Tejerina Arreal MC, Porter I, Valderas JM. Predicting Incident Multimorbidity. Annals of family medicine. 2018;16(4):322-9.
- 9. Ornstein SM, Nietert PJ, Jenkins RG, Litvin CB. The prevalence of chronic diseases and multimorbidity in primary care practice: a PPRNet report. Journal of the American Board of Family Medicine : JABFM. 2013;26(5):518-24.
- 10. Willadsen T, Jarbøl D, Reventlow S, Mercer S, Olivarius NdF. Multimorbidity and mortality: A 15-year longitudinal registry-based nationwide Danish population study. Journal ofComorbidity 2018;8:1-9.
- Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet. 2012;380(9836):37-43.

- 12. Romano E, Ma R, Vancampfort D, Firth J, Felez-Nobrega M, Haro JM, et al. Multimorbidity and obesity in older adults from six low- and middle-income countries. Prev Med. 2021.
- 13. Violan C, Foguet-Boreu Q, Flores-Mateo G, Salisbury C, Blom J, Freitag M, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. PLoS One. 2014;9(7):e102149.
- 14. Alimohammadian M, Majidi A, Yaseri M, Ahmadi B, Islami F, Derakhshan M, et al. Multimorbidity as an important issue among women: results of a gender difference investigation in a large population-based cross-sectional study in West Asia. BMJ open. 2017;7(5):e013548.
- 15. France EF, Wyke S, Gunn JM, Mair FS, McLean G, Mercer SW. Multimorbidity in primary care: a systematic review of prospective cohort studies. The British journal of general practice : the journal of the Royal College of General Practitioners. 2012;62(597):e297-307.
- Akker Mvd, Buntinx F, Metsemakers JFM, Roos S, Knottnerus JA. Multimorbidity in General Practice: Prevalence, Incidence, and Determinants of Co-Occurring Chronic and Recurrent Diseases. J Clin Epidemiol 1998;51(5):367–75.
- 17. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev 2011;10((4):430-9.
- Aiden H. Multimorbidity. Understanding the challenge. A report for the Richmond Group of Charities. 2018.
- 19. Harrison C, Henderson J, Miller G, Britt H. The prevalence of diagnosed chronic conditions and multimorbidity in Australia: A method for estimating population prevalence from general practice patient encounter data. PLoS One. 2017;12(3):e0172935.
- 20. Hunter ML, Knuiman MW, Musk BAW, Hui J, Murray K, Beilby JP, et al. Prevalence and patterns of multimorbidity in Australian baby boomers: the Busselton healthy ageing study. BMC Public Health 2021;21(1539).
- 21. Hunger M, Thorand B, Schunk M, Doring A, Menn P, Peters A, et al. Multimorbidity and health-related quality of life in the older population: results from the German KORA-age study. Health and quality of life outcomes. 2011;9:53.
- 22. NICE. Multimorbidity: clinical assessment and management: Multimorbidity: assessment, prioritisation and management of care for people with commonly occurring multimorbidity. NICE guideline NG56: National Institute for Health and Care Excellence; 2016.
- 23. Leijten FRM, Struckmann V, van Ginneken E, Czypionka T, Kraus M, Reiss M, et al. The SELFIE framework for integrated care for multi-morbidity: Development and description. Health policy (Amsterdam, Netherlands). 2018;122(1):12-22.
- 24. Charities TRGo. Just one thing after another' Living with multiple conditions: A report from the Taskforce on Multiple Conditions. . 2018.
- 25. Bayliss EA, Bonds DE, Boyd CM, Davis MM, Finke B, Fox MH, et al. Understanding the context of health for persons with multiple chronic conditions: moving from what is the matter to what matters. Annals of family medicine. 2014;12(3):260-9.

- 26. Guthrie B, Payne K, Alderson P, McMurdo MET, Mercer SW. Adapting clinical guidelines to take account of multimorbidity. BMJ (Clinical research ed). 2012;345(e6341).
- 27. Young CE, Boyle FM, Mutch AJ. Are care plans suitable for the management of multiple conditions? Journal of comorbidity. 2016;6(2):103-13.
- 28. Salisbury C, Man MS, Bower P, Guthrie B, Chaplin K, Gaunt DM, et al. Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach. Lancet. 2018;392(10141):41-50.
- 29. Ailabouni NJ, Hilmer SN, Kalisch L, Braund R, Reeve E. COVID-19 Pandemic: Considerations for Safe Medication Use in Older Adults with Multimorbidity and Polypharmacy. J Gerontol A Biol Sci Med Sci. 2020.
- 30. Guan W-j, Liang W-h, Zhao Y, Liang H-r, Chen Z-s, Li Y-m, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. The European respiratory journal. 2020.
- 31. Fortin M, Dubois MF, Hudon C, Soubhi H, Almirall J. Multimorbidity and quality of life: a closer look. Health and quality of life outcomes. 2007;5:52.
- 32. Fortin M, Lapointe L, Hudon C, Vanasse A, Ntetu AL, Maltais D. Multimorbidity and quality of life in primary care: a systematic review. Health and quality of life outcomes. 2004;2:51.
- 33. Makovski TT, Schmitz S, Zeegers MP, Stranges S, Akker Mvd. Multimorbidity and quality of life: systematic literature review and meta-analysis. Ageing research reviews. 2019.
- 34. Bao X-Y, Xie Y-X, Zhang X-X, Peng X, Huang J-X, Du Q-F, et al. The association between multimorbidity and health-related quality of life: a crosssectional survey among community middle-aged and elderly residents in southern China. Health and quality of life outcomes. 2019;17(107).
- 35. Bayliss M, Rendas-Baum R, White MK, Maruish M, Bjorner J, Tunis SL. Health-related quality of life (HRQL) for individuals with self-reported chronic physical and/or mental health conditions: panel survey of an adult sample in the United States. Health and quality of life outcomes. 2012;10(154).
- 36. Fortin M, Bravo G, Hudon C, Lapointe L, Almirall J, Dubois MF, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2006;15(1):83-91.
- 37. Lang C, Roessler M, Schmitt J, Bergmann A, Holthoff-Detto V. Health-related quality of life in elderly, multimorbid individuals with and without depression and/or mild cognitive impairment using a telemonitoring application. Quality of Life Research (2021). 2021;30:2829–41.
- Millá-Perseguer M, Guadalajara-Olmeda N, Vivas-Consuelo D, Usó-Talamantes R. Measurement of health-related quality by multimorbidity groups in primary health care. Health and quality of life outcomes. 2019;17(8).
- 39. Williams JS, Egede LE. The Association Between Multimorbidity and Quality of Life, Health Status and Functional Disability. The American journal of the medical sciences. 2016;352(1):45-52.
- 40. Hagell P, Westergren A, Årestedt K. Beware of the origin of numbers: Standard scoring of the SF-12 and SF-36 summary measures distorts measurement and score interpretations. Res Nurs Health.

2017;40:378-86.

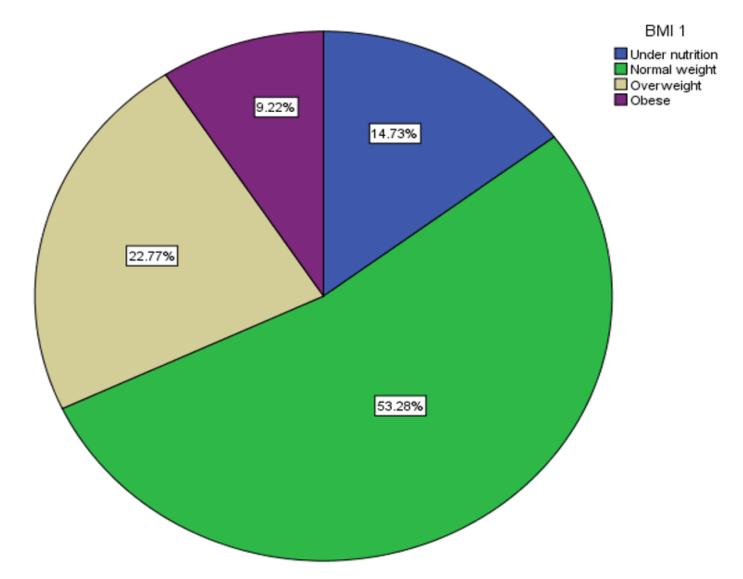
- 41. Lall R, Campbell MJ, Walters SJ, Morgan K. A review of ordinal regression models applied on healthrelated quality of life assessments. StatisticalMethods in Medical Research. 2002;11:49–67.
- 42. Lall R. The Application of Ordinal Regression Models in Quality of Life Scales used in Gerontology 2004.
- 43. Walters SJ, Campbell MJ, Lall R. DESIGN AND ANALYSIS OF TRIALS WITH QUALITY OF LIFE AS AN OUTCOME: A PRACTICAL GUIDE. ournal of Biopharmaceutical Statistics. 2001;11(3):155-76.
- 44. Liddell TM, Kruschke JK. Analyzing ordinal data with metric models: What could possibly go wrong? Journal of Experimental Social Psychology 2018;79:328–48.
- 45. McKenna SP, Heaney A. Composite outcome measurement in clinical research: the triumph of illusion over reality? Journal of medical economics. 2020;23(10):1196-204.
- 46. Abreu MNS, Siqueira AL, Cardoso CS, Caiaffa WT. Ordinal logistic regression models: Application in quality of life studies. Cad Saúde Pública, Rio de Janeiro. 2008(Sup 4):S581-S91.
- 47. Williams R. Understanding and interpreting generalized ordered logit models. The Journal of Mathematical Sociology. 2016.
- 48. Peterson B, Frank E. Harrell J. Partial Proportional Odds Models for Ordinal Response Variables. Journal of the Royal Statistical Society Series C (Applied Statistics). 1990;39(2):205-17.
- 49. Williams R. Generalized ordered logit/partial proportional odds models for ordinal dependent variables. The Stata Journal 2006;6(1):58–82.
- 50. Bürkner P-C, Vuorre M. Ordinal Regression Models in Psychology: A Tutorial. Advances in Methods and Practices in Psychological Science 1 25. 2019.
- 51. Brant R. Assessing Proportionality in the Proportional Odds Model for Ordinal Logistic Regression. Biometrics. 1990;46(4):1171-8.
- 52. Austad B, Hetlevik I, Mjolstad BP, Helvik AS. Applying clinical guidelines in general practice: a qualitative study of potential complications. BMC family practice. 2016;17:92.
- 53. Turner A, Mulla A, Booth A, Aldridge S, Stevens S, Begum M, et al. The international knowledge base for new care models relevant to primary care-led integrated models: a realist synthesis. HEALTH SERVICES AND DELIVERY RESEARCH. 2018;6 (25).
- 54. Eyowas FA, Schneider M, Alemu S, Getahun FA. Multimorbidity of chronic noncommunicable diseases: burden, care provision and outcomes over time among patients attending chronic outpatient medical care in Bahir Dar, Ethiopia—a mixed methods study protocol. BMJ-Open. 2021;11(9):e051107.
- 55. Bank TW. Public Expenditure and Financial Accountability (PEFA): Amhara National Regional Government. 2020.
- 56. G/Michael M, Dagnaw W, Yadeta D, Feleke Y, Fantaye A, Kebede T, et al. Ethiopian National Guideline on Major NCDs 2016. 2016.

- 57. Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial A Report from the WHOQOL Group. Quality of Life Research 2004;13:299–310.
- 58. Gonzalez-Chica DA, Hill CL, Gill TK, Hay P, Haag D, Stocks N. Individual diseases or clustering of health conditions? Association between multiple chronic diseases and health-related quality of life in adults. Health and quality of life outcomes. 2017;15(1):244.
- 59. Carlozzi NE, Kratz AL, Downing NR, Goodnight S, Miner J, Migliore N, et al. Validity of the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) in individuals with Huntington disease (HD). Quality of Life Research 2015;24(8):1963-71.
- WARE JEJ, KOSINSKI MM, KELLER SD. A 12-Item Short-Form Health Survey: Construction of Scales and Preliminary Tests of Reliability and Validity. Ovid: WARE : Med Care, Volume 34(3)March 1996. 1996;34(3):220-33.
- 61. Lawson KD, Mercer SW, Wyke S, Grieve E, Guthrie B, Watt GC, et al. Double trouble: the impact of multimorbidity and deprivation on preference-weighted health related quality of life a cross sectional analysis of the Scottish Health Survey. International journal for equity in health. 2013;12(68).
- 62. Stubbs B, Vancampfort D, Veronese N, Kahl KG, Mitchell AJ, Lin PY, et al. Depression and physical health multimorbidity: primary data and country-wide meta-analysis of population data from 190 593 people across 43 low- and middle-income countries. Psychological medicine. 2017;47(12):2107-17.
- 63. Kocalevent R-D, Berg L, Beutel ME, Hinz A, Zenger M, Härter M, et al. Social support in the general population: standardization of the Oslo social support scale (OSSS-3) BMC Psychology volume 6, Article number: 31 (2018). 2018.
- 64. FAO. Wealth Index mapping in the Horn of Africa. Animal Production and Health Working Paper. No.4. Rome. 2011.
- 65. Chakraborty NM, Fry K, Behl R, Longfielda K. Simplified Asset Indices to Measure Wealth and Equity in Health Programs: A Reliability and Validity Analysis Using Survey Data From 16 Countries. Global Health: Science and Practice 2016;4(1).
- 66. Abebe F, Schneider M, Asrat B, Ambaw F. Multimorbidity of chronic non-communicable diseases in low- and middle-income countries: A scoping review. Journal ofComorbidity 2020;10:1–13.
- 67. WHO. Process of translation and adaptation of instruments. 2014.
- 68. Hall DA, Domingo SZ, Hamdache LZ, Manchaiah V, Thammaiah S, Evans C, et al. A good practice guide for translating and adapting hearingr elated questionnaires for different languages and cultures. International Journal of Audiology 2018;57:161–75.
- 69. OCHA. Manual Kobo Toolbox. https://www.kobotoolbox.org/: Office for the Coordination of Humanitarian Affairs (OCHA) in West and Central Africa; 2019 [
- 70. Sasidharan L, Menéndez M. Partial proportional odds model—An alternate choice for analyzing pedestrian crash injury severities. Accident Analysis and Prevention 2014;72(14): 330–40.
- 71. Fullerton AS, Xu J. The proportional odds with partial proportionality constraints model for ordinal response variables. Social Science Research. 2012;41(1):182-98.

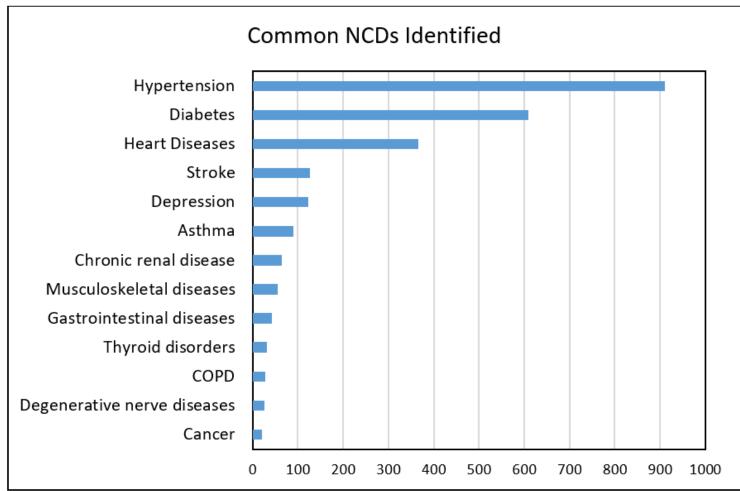
- 72. AMS. Multimorbidity: a priority for global health research. 2018.
- 73. Tisminetzky M, Bayliss EA, Magaziner JS, Allore HG, Anzuoni K, Boyd CM, et al. Research Priorities to Advance the Health and Health Care of Older Adults with Multiple Chronic Conditions. J Am Geriatr Soc. 2017;65(7):1549-53.
- 74. Abreu MNS, Siqueira AL, Cardoso CS, Caiaffa WT. Ordinal logistic regression models: application in quality of life studies. Cad Saúde Pública 2008;24(suppl 4).
- 75. WHO. World report on ageing and health. 2015.
- 76. Makovski TT, Schmitza S, Zeegers MP, Stranges S, Akker Mvd. Multimorbidity and quality of life: Systematic literature review and metaanalysis. Ageing research reviews. 2019;53.
- 77. Kanesarajah J, Waller M, Whitty JA, Mishra GD. Multimorbidity and quality of life at mid-life: A systematic review of general population studies. Maturitas. 2018;109:53-62.
- 78. Prazeres F, Santiago L. Relationship between health-related quality of life, perceived family support and unmet health needs in adult patients with multimorbidity attending primary care in Portugal: a multicentre cross-sectional study. Health and quality of life outcomes. 2016;14(1):156.
- 79. Michelson H, Bolund C, Brandberg Y. Multiple Chronic Health Problems are Negatively Associated with Health Related Quality of Life (HRQoL) irrespective of Age. Quality of Life Research. 2000;9(10):1093-104.
- 80. Garin N, Koyanagi A, Chatterji S, Tyrovolas S, Olaya B, Leonardi M, et al. Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study, J Gerontol A Biol Sci Med Sci. J Gerontol A Biol Sci Med Sci. 2016;71 (2):205-14.
- 81. Garin N, Olaya B, Moneta MV, Miret M, Lobo A, Ayuso-Mateos JL, et al. Impact of multimorbidity on disability and quality of life in the Spanish older population. PLoS One. 2014;9(11):e111498.
- 82. Vogel I, Miksch A, Goetz K, Ose D, Szecsenyi J, Freund T. The impact of perceived social support and sense of coherence on health-related quality of life in multimorbid primary care patients. Chronic illness. 2012;8(4):296–307.
- 83. Demirer I, Bethge M, Spyra K, Karbach U, Pfaffe H. Does social support mediate the effect of multimorbidity on mental wellbeing in the German working population? A longitudinal mediation analysis using structural equation modelling. SSM - population health. 2021;13(100744).
- 84. Scha[¬]fer I, Hansen H, Kaduszkiewicz H, Bickel H, Fuchs A, Gensichen J, et al. Health behaviour, social support, socio-economic status and the 5-year progression of multimorbidity: Results from the MultiCare Cohort Study. Journal ofComorbidity 2019;9:1–11.
- 85. Ryan A, Wallace E, O'Hara P, Smith SM. Multimorbidity and functional decline in community-dwelling adults: a systematic review. Health and quality of life outcomes. 2015;13:168.
- 86. Rivera-Almaraz A, Manrique-Espinoza B, Ávila-Funes JA, Chatterji S, Naidoo N, Kowal P, et al. Disability, quality of life and all-cause mortality in older Mexican adults: association with multimorbidity and frailty. BMC geriatrics. 2018;18(236).
- 87. Subramaniam M, Zhang Y, Lau JH, Vaingankar JA, Abdin E, Chong SA, et al. Patterns of physical activity and healthrelated quality of life amongst patients with multimorbidity in a multi-ethnic Asian

population. BMC Public Health. 2019;19(1612).

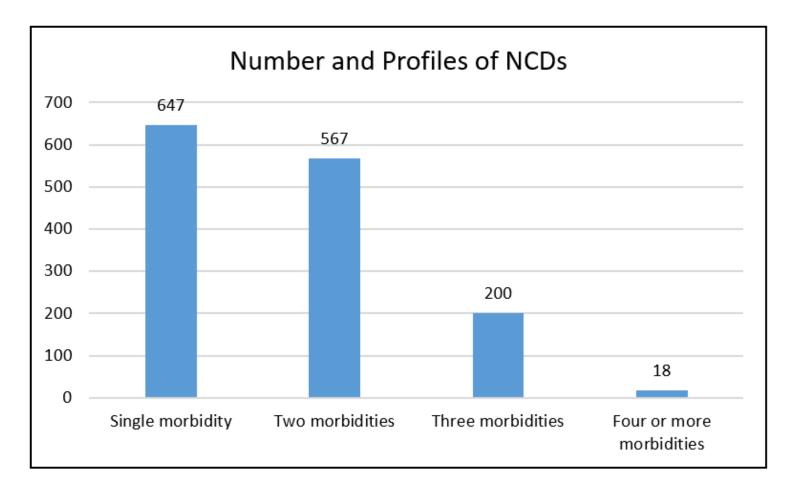
- 88. Kuipers SJ, Cramm JM, Nieboer AP. The importance of patient-centered care and co-creation of care for satisfaction with care and physical and social well-being of patients with multi-morbidity in the primary care setting. BMC health services research. 2019;19(13).
- 89. Smith SM, Wallace E, O'Dowd T, Fortin M. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. The Cochrane database of systematic reviews. 2016;3:CD006560.
- 90. Smith SM, Wallace E, Salisbury C, Sasseville M, Bayliss E, Fortin M. A Core Outcome Set for Multimorbidity Research (COSmm). Annals of family medicine. 2018;16(2):132-8.
- 91. Valderas JM, Gangannagaripalli J, Nolte E, Boyd CM, Roland M, Jones AS-SE, et al. Quality of care assessment for people with multimorbidity, scoping review. 2019.



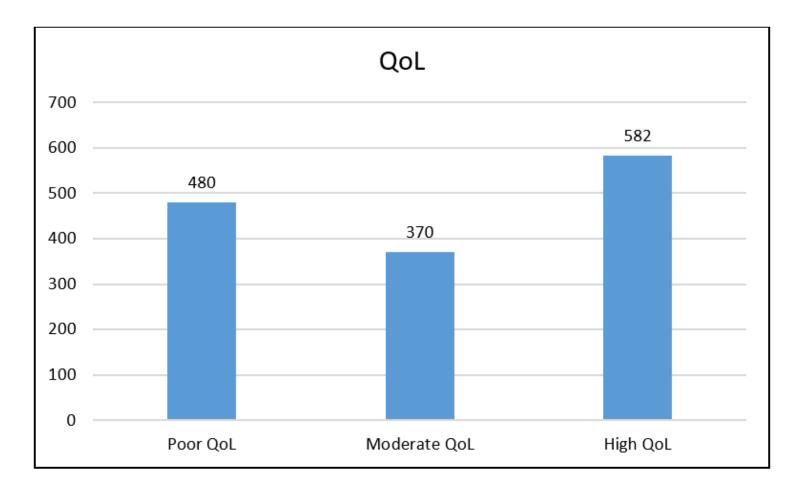
Figures



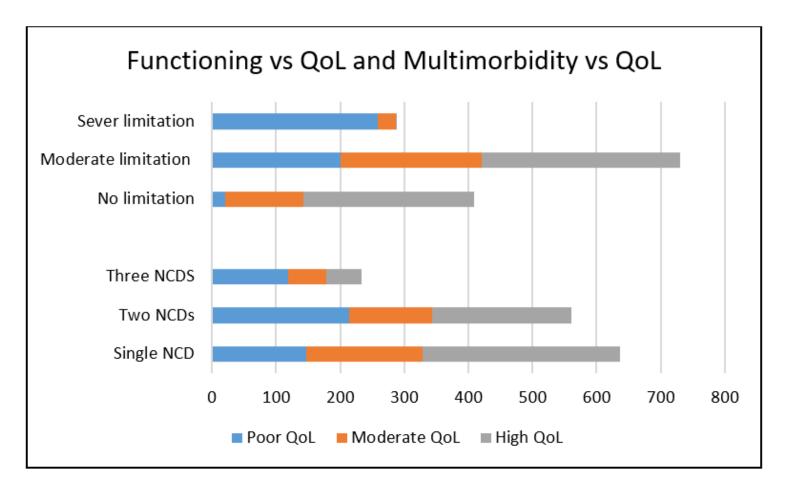
List of NCDs studied and their magnitude among participants attending chronic outpatient NCDs care, Bahir Dar, Ethiopia (N=1432)



Patterns of NCDs morbidity among individuals attending chronic NCDs care in Bahir Dar, Ethiopia (N=1432)



Number of individuals classified in different categories of health-related QoL



Graphic presentation of the relationship between QoL, functioning and multimorbidity