BMJ Open Multimorbidity of chronic non-communicable diseases: burden, care provision and outcomes over time among patients attending chronic outpatient medical care in Bahir Dar, Ethiopia – a mixed methods study protocol

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ABSTRACT

Introduction Multimorbidity refers to the presence of two or more chronic non-communicable diseases (NCDs) in a given individual. It is associated with premature mortality, lower quality of life (QoL) and greater use of healthcare resources. The burden of multimorbidity could be huge in the low and middle-income countries (LMICs), including Ethiopia. However, there is limited evidence on the magnitude of multimorbidity, associated risk factors and its effect on QoL and functionality. In addition, the evidence base on the way health systems are organised to manage patients with multimorbidity is sparse. The knowledge gleaned from this study could have a timely and significant impact on the prevention, management and survival of patients with NCD multimorbidity in Ethiopia and in LMICs at large.

Methods and analysis This study has three phases: (1) a cross-sectional quantitative study to determine the magnitude of NCD multimorbidity and its effect on QoL and functionality, (2) a qualitative study to explore organisation of care for patients with multimorbidity, and (3) a longitudinal quantitative study to investigate disease progression and patient outcomes over time. A total of 1440 patients (≥40 years) on chronic care follow-up will be enrolled from different facilities for the quantitative studies. The quantitative data will be collected from multiple sources using the KoBo Toolbox software and analysed by STATA V.16. Multiple case study designs will be employed to collect the qualitative data. The qualitative data will be coded and analysed by Open Code software thematically.

Ethics and dissemination Ethical clearance has been obtained from the College of Medicine and Health Sciences, Bahir Dar University (protocol number 003/2021). Subjects who provide written consent will be recruited in the study. Confidentiality of data will be strictly maintained. Findings will be disseminated through publications in peer-reviewed journals and conference presentations.

Strengths and limitations of this study

- This is the first facility-based study on the magnitude and impacts of multimorbidity on patients with chronic non-communicable diseases in the country.
- This study is also the first in low and middle-income countries to analyse disease progression and outcomes of patients with multimorbidity over time.
- Further, this study will qualitatively explore health service provision and lived experience of patients with multimorbidity.
- However, findings from facility-based studies may not be generalisable to the underlying characteristics in the general population.
- In addition, the COVID-19 pandemic may affect patterns of patient follow-up in our study signalling cautious generalisability of the findings to other contexts in the country.

BACKGROUND

Chronic non-communicable diseases (NCDs) are the diseases of everyone, long lasting, could occur at any age, no cure and are often the cause of death of the people living with NCDs.¹ Making the issue more challenging, they are occurring in combination of two or more, a condition known as multimorbidity.² Multimorbidity often refers to the simultaneous occurrence of two or more chronic conditions in a given person.^{2,3} It is a growing problem posing significant challenges to health systems around the world.⁴

Global prevalence estimates of multimorbidity of chronic conditions vary from 3.5% to 98.5% in primary care patients and from 13.1% to 71.8% among the general

population.⁵ Higher prevalence estimates were observed in high-income countries (HICs), where about one in four adults experience multimorbidity.³ The burden of NCD multimorbidity is also rising in low and middle-income countries (LMICs).^{6,7} Based on our recent review, the prevalence of multimorbidity ranged from 3.2% to 90.5% across studies in LMICs.⁸ The wide interval in the prevalence estimates across studies was attributed to marked variations in the methodologies employed to define and measure multimorbidity.^{5,9}

Studies were heterogeneous in terms of age of the participants involved, the type and number of chronic conditions considered, study setting, methods of data collection and sources of data used to define multimorbidity.^{5,9} Use of different methodologies resulted in differences in prevalence rates and difficulty in comparing and pooling the estimates.^{5,10}

Although multimorbidity has consistently been increasing with age,^{4,11–14} it is also socially patterned, where a higher prevalence and much earlier occurrence is observed among socioeconomically deprived populations than their wealthier counterparts.¹⁴ Patients living in deprived areas are also particularly vulnerable to multimorbidity that includes mental health conditions such as depression.¹⁵ In addition, women were more likely than men to have higher odds of multimorbidity.^{10,16} Further, individual lifestyle factors including unhealthy diet and obesity,⁹ physical inactivity,^{9,17} harmful use of alcohol,¹¹ tobacco smoking¹⁸ and psychosocial factors, such as negative life events and believing in external locus of control were also factors associated with multimorbidity.^{19,20} Interestingly, Sturmberg and colleagues²¹ described the whole chain of mechanisms that may be involved in the pathophysiology of multimorbidity, spanning from the genome up to the biological level and from the human scale to the level of individuals, environment and society.

Living with multimorbidity is associated with disability, lower quality of life (QoL) and premature mortality.^{3,22} In addition, people with multiple chronic conditions are more likely than their counterparts to experience higher rate of hospital admission and related health and social care costs.³

People living with multimorbidity need more holistic, generalist long-term care and support than patients having a single NCD.²³ They are also high users of health-care resources.²⁴ However, most patients with multiple chronic conditions may have more than one physician, such as one from each relevant specialty often working in silos and are prescribed with more drugs (polypharmacy) for long periods of time often leading to dangerous drug interactions and complications.²⁵ They also face challenges in navigating the healthcare system and managing their health, and are generally less satisfied with the care they receive.³ Further, the rapid emergence of infections such as COVID-19 is fuelling the complexity and posing a huge burden to the health systems and worsening outcomes of patients with pre-existing chronic diseases and multimorbidity.^{26,27}

The impact of multimorbidity is likely to be significant in LMICs, including Ethiopia where health systems are overwhelmed by the high speed of NCD growth and high burden of communicable diseases such as HIV, Tuberculosis and malaria.² On the other hand, health systems in LMICs are largely configured with conventional one-size-fits-all chronic care model rather than designing a model of care for every possible combination of chronic conditions.²⁸ Perhaps, access to NCD care is inadequate to the poor, furthering disease accumulation and long-term complications, including financial crises.³

The evidence base for determining the most effective ways to treat patients living with several medical conditions is thin.²⁸ Although it has been impossible to generate an ideal model of care for every possible combination of chronic conditions across different contexts, a range of guiding principles^{3,23} and intervention models²⁹ are evolving. The notion of patient-centredness and integration remain common among the differing models of multimorbidity care being implemented.^{30,31} Evidence showed that the patient-centred medical homes,³² the Salford Integrated Care Programme,³³ the whole system intervention (CARE Plus)³⁴ and patient activation (PA) system³⁵ are effective in improving patient outcomes. However, the Dimension of care, Depression and Drugs model,^{36,37} the telemonitoring in community centres model³⁸ and the patient-centred care model³⁹ did not show a significant improvement in the outcomes of patients with multimorbidity in HICs.

However, there is no evidence on the most effective ways to treat patients living with several chronic medical conditions in LMICs.^{40,41} Therefore, it is likely that patients with multimorbidity face accumulating and overwhelming complexity resulting from the sum of uncoordinated responses to each of their health problems.^{24,42,43} In addition, currently, the emergence of the coronavirus infection is demanding a change in the way patients with chronic conditions and multimorbidity are managed and followed.^{26,27} Failing to do so will increase the risk of dying due to COVID-19 among people living with chronic medical conditions and multimorbidity.⁴⁴

Despite the huge challenge multimorbidity brings, there is a significant information gap in terms of the burden, associated risk factors, its effect on QoL and functionality and outcomes of patients over time in Ethiopia. Moreover, there is no evidence on the lived experiences of patients with multimorbidity and how the current health system is organised to manage patients with multimorbidity. The knowledge gleaned from this study may have a timely and significant impact on the prevention, management and survival of patients with NCD multimorbidity in the country and in LMICs at large. This study will also serve as a baseline for shaping future research endeavours in the field.

The figure below (figure 1) is a conceptual framework showing the interplay between risk factors of multimorbidity and its relationship with important patient

Figure 1 Conceptual framework of the risk factors and outcomes of multimorbidity (Modified from the WHO's Determinants of Health and Their Impacts on Chronic Diseases Conceptual Framework. Epidemiology and prevention of chronic non-communicable diseases)⁴⁵ Antiretroviral Therapy (ART), Quality of Life (QoL), Human Immunodeficiency Virus (HIV), Non-Communicable Diseases (NCDs).

outcomes and health service delivery. It was developed based on the WHO's NCD conceptual framework.⁴⁵

OBJECTIVES

The proposed study aimed to address the following objectives:

1. To determine the magnitude of NCD multimorbidity and associated factors among patients attending chronic outpatient NCD care.
2. To determine the effects of multimorbidity on QoL and functionality of patients with multimorbidity.
3. To determine disease progression and outcomes of patients with NCD multimorbidity over time (measured as occurrence of new disease/s, mortality and changes in QoL and functionality from the baseline values).
4. To explore how the care of patients with NCD multimorbidity is organised.

METHODS AND ANALYSIS

Study design

This is a multicentre mixed methods study to be conducted in three consecutive phases: (1) a multicentre cross-sectional quantitative study to determine the magnitude and effect of multimorbidity on QoL and functionality, (2) a qualitative study to explore the way service delivery is organised to manage patients with multimorbidity, and

(3) a longitudinal study to analyse the disease course and outcomes of patients over time.

Study settings

This study will be conducted in hospitals (both public and private) and private higher/specialty clinics in Bahir Dar city, north-west Ethiopia. Majority (~80%) of the individuals living with chronic conditions in the city and surrounding residences receive NCD care from these facilities in a relatively uniform fashion. Chronic NCD care and management in Ethiopia follow the national NCD treatment guideline.⁴⁶ However, access to comprehensive chronic NCD care packages in the study area is inadequate and expensive in public and private health facilities, respectively.

Source population

Older adults (≥40 years) having at least one of the chronic NCDs/conditions in Ethiopia.

Study population

Adult patients (≥40 years) attending chronic care in hospitals and higher/specialised clinics in Bahir Dar city.

Study period

The study will be conducted from March 2021 to February 2022. The quantitative data will be collected at baseline (March to April, 2021), at 6 months (September to October, 2021) and at the end of 1 year

of follow-up (February, 2022), while the qualitative data will be collected after the baseline assessment (August to September, 2021).

Selection of health facilities

Only facilities who have been providing chronic NCD care by general practitioners or specialist physicians for at least a duration of 1 year prior to the data collection period will be considered.

Study participants

Older adults (40 years or more) diagnosed with at least one NCD and are on chronic diseases follow-up care for at least 6 months prior to the study period will be enrolled for the study.

Exclusion criteria

Pregnant women will be excluded because they may have pregnancy-induced chronic conditions, including hypertension, diabetes and heart disease, etc. In addition, patients who are severely ill to be interviewed and admitted patients will be excluded. This is to avoid the inconveniences we might encounter during assessment of physical indices, such as height, weight, waist circumference, hip circumference and interview sessions.

Sample size

Key issues considered to estimate the minimum sample size required for the quantitative study were study objectives, nature of the dependent variables and key predictor variables, study designs (cross-sectional vs repeated measures longitudinal) and analysis technique (binary logistic regression, generalised estimating equation (GEE) or mixed model). However, the input values: α (type I error=0.05), power ($1-\beta=90$), confidence level (95%) and an estimated non-response and attrition during follow-up (20%) remain constant while using different formulas.

We found the general linear multivariate model with Gaussian errors (GLIMMSE) sample size and power calculator^{47–49} as an appropriate method to yield the maximum sample size required for the study using simulated inputs compared with the sample size calculated for the primary response variable using single population proportion formula (considering 50% prevalence rate and a 0.05 margin of error).

We aimed to detect a 5 points average score difference in terms of QoL between patients having single NCD and patients with NCD multimorbidity (those having two or more chronic conditions had a lower score).⁵⁰ A 5 points score difference is considered clinically important.⁵¹

Based on the given assumptions and the formula we used to estimate the sample size, the sample size required became 600. As the nature of participants is likely to be different by the type of facility (public or private) they receive care (figure 2), we will employ stratification to ensure fair representation in the sample for important subgroups that may differ in significant ways or have an effect on the dependent variables being studied. Hence, a design effect of 2 will be considered because participants

are clustered in health facilities to avoid possible loss during stratification giving rise to a required sample of 1200. Adding 20% to the possible loss to follow-up and non-response, the total sample size required both for the cross-sectional and longitudinal studies will be 1440.

OPERATIONAL DEFINITION AND MEASUREMENT OF VARIABLES

Primary dependent variable

Multimorbidity is operationalised as the co-occurrence of two or more chronic diseases (hypertension, diabetes, depression, heart attack, angina, stroke, heart failure, asthma, Chronic Obstructive Pulmonary Disease (COPD), cancer and up to three additional self-reported chronic conditions) in a given individual.⁵² These disease conditions were selected based on the information obtained from a published scoping review⁸ and a review of 210 randomly selected patient charts from two primary care hospitals providing chronic care in the study area. Moreover, based on a pilot study conducted, data on six other prevalent ($\geq 1\%$) chronic diseases in the study area, including arthritis, low back pain, hyperthyroidism, chronic kidney disease, chronic liver disease and Parkinson's disease, will be collected. Information about these diseases will be captured from different sources (chart review, patient interview and assessment of physical and laboratory data). A validated version of the Multimorbidity Assessment Questionnaire for Primary Care (MAQ-PC)⁵³ will be used to capture the data on multimorbidity.

Assessment of chronic diseases

Data on the presence of hypertension, diabetes, heart diseases (heart failure, angina and heart attack), stroke, asthma, COPD and cancer will be obtained from self-report (interview) data and review of medical records. When combined, these methods provide adequate information on presence of chronic medical conditions^{54 55} and considering 8–12 chronic conditions was supposed to be sufficient to estimate multimorbidity in a stable way.⁵⁴ Direct assessment of the mentioned chronic conditions is not possible due to resource constraints and methodological challenges.

The tendency to report presence of depression among clients is seemingly low (due to fear of stigma), and if they do report symptoms, it will be difficult to classify the degree of severity of self-report data.⁵⁶ Hence, we will assess it objectively through an interview using the Patient Health Questionnaire (PHQ-9). PHQ-9 is validated in Ethiopia.^{57 58} Possible PHQ-9 scores range from 0 to 27 and patients scoring 10 or more will be classified as having depression. Medical records will also be reviewed for a doctor-diagnosed depression disorder.

Secondary dependent variables

Health-related QoL

Health-related QoL is defined as an individual's perception of their position in life in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns.⁵⁹ QoL will

Figure 2 Schematic presentation of how eligible health facilities were stratified and the sample size to be drawn from each participating facility, Bahir Dar, Ethiopia.

be measured using interviewer-administered Short Form (SF-12) assessment tool.^{60 61} The tool is extensively validated and widely used generic tool for measuring QoL in multimorbidity across different contexts.^{50 62} The scores may range from 0 to 100, 0 representing worst health.⁵¹

Level of disability

Level of disability (functional status) will be measured using the WHO's 12-item Disability Assessment Schedule (WHODAS 2.0) tool.^{61 63} Functional limitation will be used as a proxy for diseases severity. The responses to the items in the WHODAS tool will be used to construct disease severity as a latent outcome variable. Respondents will be asked to state the level of difficulty experienced taking into consideration how they usually do the activity, including the use of any assistive devices and/or the help of a person. In each item, individuals have to estimate the magnitude of the difficulty they had during the previous 30 days using a 5-point scale (none=1, mild=2, moderate=3, severe=4, extreme/cannot do=5). The results of the 12 items will be summed up to obtain a global score expressed on a continuous scale from 0 (no disability) to 100 (full disability). The 12-item WHODAS 2.0 has been validated and used in Ethiopia.⁶⁴

Independent variables

Independent variables include sociodemographic characteristics (age, gender, education, wealth index, marital status, family size, residence and occupation), dietary habits (amount and frequency of fruit and vegetables consumption, amount of daily salt consumption and types of oil and fat used for cooking), behavioural and lifestyle patterns (alcohol consumption, smoking, khat consumption, physical exercise), HIV infections, body mass index (BMI), waist and hip circumferences, PA status, social support system and locus of control.

Measurement of BMI, waist-to-hip ratio, PA, social support system, locus of control and wealth index

Height and weight will be measured using standardised techniques with participants barefoot and wearing light clothing. Participants' height will be measured to the nearest 0.1 cm using a portable Seca 213 Stadiometer and weight will be recorded to the nearest 0.1 kg using a weighing scale. These data will be used to calculate individual BMI (kg/m^2). BMI values will be classified into categories for each individual based on established WHO cut-offs for BMI, which included four categories:

underweight ($<18.5 \text{ kg/m}^2$), normal ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25.0\text{--}29.9 \text{ kg/m}^2$) and obese (30 kg/m^2).⁶⁵

A flexible, stretch-resistant tape will be used to measure waist and hip circumference to the nearest 0.1 cm midway between the 12th rib and the iliac crest and around the widest portion of the hips, respectively. For both measurements, the individual will stand with feet close together, arms at the side and body weight evenly distributed, and wear light clothing. Each measurement will be repeated twice and the average will be calculated given that the difference between the two measurements does not exceed 1 cm. Then, waist-to-hip ratio will be calculated and interpreted according to the WHO's protocol.⁶⁶

PA will be assessed using validated tools.^{67 68} The tool contains 13 statements answered on a 4-point Likert-type scale about managing one's health and summed to a 100-point scale, with higher scores reflecting higher levels of activation.⁶⁹

Social networking and support system will be assessed through face-to-face interview using pretested and standardised tools (Oslo Scale).⁷⁰ A scale ranging from 3 to 8 will be interpreted as poor social support, 9–11 moderate social support and 12–14 strong social support. Multi-dimensional health locus of control scale (form C) will be used to assess health-related control beliefs (locus of control) of the people living with chronic NCDs.⁷¹ The 18-item scale will be scored using Likert scale as strongly agree (6 points) to strongly disagree (1 point).

Wealth index (a latent construct) at household level will be generated from a combination of material assets and housing characteristics.⁷² The wealth index will be scored using principal component analysis (PCA) technique. The score will be classified into quintiles, quintile 1 represents the poorest and quintile 5 the wealthiest.⁷³

Sampling technique

A two-stage clustered stratified random sampling method was adopted for recruiting facilities and participants. Facilities are stratified into two strata as public and private and we grouped them based on their level of specialty (figure 2). Assuming patients are regularly visiting the same facility, and that there is a relatively homogeneous subpopulation in each level, facilities were randomly selected from each category. The sample size from each facility has been determined based on the notion of probability proportional to size using the pool of patients with chronic NCD (≥ 40 years) registered for follow-up over

the year preceding our assessment (January to December 2020) in each participating facility. Moreover, looking into the daily average volume of patients visiting each facility, we anticipate that the required sample of patients from each participating facility could be recruited in 1-month period. We will be employing a systematic random sampling technique to select eligible participants from the list of patients attending chronic care follow-up on each working day from 15 March to 30 April 2021.

Table 1 shows the facilities which have been randomly selected and the number of participants to be enrolled from each selected facility was determined based on the annual volume of patients they had over the past 1 year preceding our study.

Data collection tools and procedures

For the sake of a more efficient and accurate data collection, aggregation and statistical analysis, the data will primarily be collected by the KoBo Toolbox software.⁷⁴ The questionnaire designed in Microsoft Word will be installed on smartphone devices after being validated and pilot tested in the field. Testing of the data entry system will be made before the actual data collection. The data will be collected offline in the field and sent directly to the server online daily. However, hard copies of the tools will be provided when data collectors face a glitch in using and navigating the platform, usually due to power outages (of mobile devices). Unique identifiers (ID) will be given to each participant and instruments will be coded with corresponding IDs to allow linkage/matching to measurement/assessment data (interview, chart review and physical assessment) relating to that participants.

Patients will be interviewed and assessed following consultation periods. Physicians and nurses working in the chronic care unit will be involved in the data collection process. However, data will be primarily collected by graduate nurses recruited from institutions outside the study facilities.

Data will be collected in three steps. First, information on sociodemographic characteristics, dietary practices, lifestyle habits, doctor-diagnosed medical condition/s, QoL, functionality, activation status (PA), psychosocial support, locus of control and depression level will be collected by face-to-face interview. Then, measurement of weight, height and waist circumference will be made. Finally, patient charts (medical records) will be reviewed to capture recorded medical diagnoses, medications

Table 1 Number of patients to be enrolled from each participating health facility, Bahir Dar

Public facilities			Private facilities				
Addisalem Primary Hospital	Felegehiwot Specialized Hospital	Tibebe Ghion Specialized Teaching Hospital	GAMBY General Hospital	Adinas General Hospital	Eyasta Specialty Clinic	Biruk Specialty Clinic	Kidanemihret Specialty Clinic
156	400	336	120	100	135	116	77
Total							1440

prescribed (for hypertension, diabetes, depression, heart attack, angina, heart failure, stroke, COPD, asthma and cancer), Fasting Blood Glucose (FBG), Glycated Hemoglobin (HbA1c) and HIV status.

When combined, self-report data and review of medical records are sufficient to yield accurate information on presence of chronic medical conditions.^{54 55} Other than the diseases identified above, patients will be prompted to list up to three chronic illnesses they are living with if any. In addition, data on COVID-19 infection will also be gathered at different points in time through patient interview and review of medical records and no direct assessment of COVID-19 infection will be made due to resource constraints and methodological challenges.

The total time a participant is expected to spend in the study is 25–30 min (20 min for interview and 5–10 min for measuring weight, height, waist and hip circumferences). Before enrolment, eligible participants will be notified (using the information sheet) about the length of time they will be staying with us and the type of data we will be collecting from them.

Data quality assurance

The fact that we will be using KoBo Toolbox software to collect the data, errors will be minimised and real-time data validation can be made as data are collected.⁷⁴ The questionnaires to measure multimorbidity, PA, social support system and locus of control will be adapted and translated to Amharic (local language) for cross-cultural adaptability based on standard protocols.^{75 76} Since there is no validated tool to measure multimorbidity in Ethiopia, we sought permission to adapt, validate and use the MAQ-PC tool which was developed and tested by Pati and colleagues in India.⁷⁷ Two primary care physicians and three experts will be consulted to respond to the questionnaire to obtain an initial impression of how easy the MAQ-PC questions are to read out, understand and answer. We will then conduct a Delphi technique involving researchers, doctors and nurses to assess the face and content validity of the Amharic version of the instruments to be used the first time in Ethiopia, including the MAQ-PC, the SF-12 QoL assessment tool, the PA measuring tool and the tools to measure social support system and locus of control. In addition, to understand how respondents perceive and interpret questions (in the new tools) and to identify potential problems that may arise during interview process, cognitive interviews will be conducted among 12 conveniently selected adult patients with chronic NCD of diverse ages and socioeconomic status (six men and six women). Cognitive interviews have been used in a number of areas in healthcare research to pretest and validate questionnaires and to ensure high response rates.⁷⁸ The questionnaires to measure QoL, functional limitation, depression and sociodemographic, dietary and lifestyle characteristics were, however, translated, validated and used across different cultures in Ethiopia, and hence we will only do pilot testing of these instruments.

All the tools will be preloaded into KoBo Toolbox software and piloted using 2% of the sample (n=29) in one public hospital and one private hospital which will not be involved in the main study.

Data collectors and supervisors will receive a high level of training detailing the study, including obtaining written consent, record review, conducting face-to-face interview, performing physical measurement and filling the questionnaire. In addition, data collectors and supervisors will receive training on the use of KoBo Toolbox software and mobile technology.

The data collection process will be monitored by trained supervisors and the principal investigator (PI). In addition, the data sent every day to the server will be checked for completeness, accuracy and clarity.

Patients registered in more than one facility will only be enrolled in the facilities where the patients had regular follow-up. Contact details of patients involved in the study will be documented to contact them during the follow-up studies. Using the KoBo Toolbox software would help matching of the longitudinal data easier.⁷⁴

Data analysis

Data will be further cleaned and analysed by STATA V.16. Descriptive statistics will be computed to describe the sociodemographic, lifestyle and other characteristics of participants and to summarise the distribution of multimorbidity and independent variables. Multimorbidity of selected chronic conditions will be assessed through combining information from different sources. The prevalence of multimorbidity among patients will be determined by calculating the proportion of patients having two or more of chronic NCDs. We will be conducting a latent class analysis (LCA) to identify the subgroups of patients sharing characteristics and to determine the patterns of multimorbidity of chronic NCDs in the study area. Determinants of NCD multimorbidity will be examined using logistic regression with multimorbidity as a dependent variable, and sociodemographic characteristics, dietary, lifestyle and physical measurement data, laboratory data, PA, perceived social support and locus of control as predictors. The patterns of multimorbidity generated from the LCA will be fitted to ordinal logistic regression model so as to determine the effect of multimorbidity on important patient outcomes such as QoL and functionality.

QoL will be computed and interpreted as a continuous variable. Descriptive analysis will be run to estimate mean and SD. Multiple linear regression analysis will be employed to identify correlates. Multilevel models will be fitted to test the simultaneous effect of individual and group-level variables on the outcome. We will analyse the association of patient characteristics with QoL by multilevel mixed-effects linear regression allowing for random effects. Patterns of multimorbidity will be constructed and treated as group-level variable through aggregation and participants' sociodemographic characteristics will be used as explanatory variables at a lower level.

Disability will be treated as categorical variable (no disability, mild disability, moderate disability and severe disability) and ordinal logistic regression will be employed to identify associated factors.

Measurement and analysis of the longitudinal data

Outcomes of patients will be assessed at 6 months and 1 year of follow-up using QoL as a primary outcome variable and functionality, disease progression and mortality as secondary outcome variables. In addition to assessing the progress and outcomes of patients over time, study variables (sensitive to change over time) measured at baseline will be measured longitudinally (at 6 months and at 1 year of the follow-up) using the methods and tools employed at baseline.

The data from the KoBo Toolbox server will be exported to an Excel spreadsheet to visualise all the information entered, including the date and time each study subject is recruited. Based on this information, we will determine the time of enrolment at 6 months and at 1 year of the follow-up period. Patients will be notified about the time when we would be contacting them for the follow-up studies. Patient contact information such as telephone/mobile number will be recorded for communicating with patients during the follow-up period.

GEE model will be fitted to assess incidence and trend of the outcomes over time and identify factors associated. In addition, multilevel (mixed effects) modelling will be fitted to understand the effect of individual-level and group-level variables on QoL by putting the sociodemographic characteristics at level 2 and multimorbidity patterns at level 1. Other outcome such as mortality will be analysed by descriptive statistics. To determine the relationship and the simultaneous effect of one or more variables on the outcome variables, we will be fitting a structural equation modelling.⁷⁹ All the necessary assumptions will be tested for the statistical models we will be fitting and estimates will be considered as significant if $p < 0.05$.

METHODS AND ANALYSIS FOR THE QUALITATIVE STUDY

Design

Multiple case study design will be employed to gain an in-depth and holistic understanding of the management practice of multimorbidity, with data needing to converge in a triangulating fashion. The case study approach will incorporate a number of data sources to provide the level of detail, necessary to provide a 'thick' description of the case. The case study approach is a suitable methodology for illuminating the complexities inherent in researching the social system of organisation.⁸⁰ However, a phenomenological design will be employed to explore the lived experiences of patients with multimorbidity.

As propositions are needed to direct the areas that should be explored within the scope of the case study,⁸¹ the following propositions are considered. These

propositions were crafted based on the knowledge and practice of service provision contained within the literature.

1. How services are delivered is dependent on how practice staff understand the matter, what is needed and what is possible given the context.
2. Managing the care of patients with multiple conditions is constrained by the way services are commonly configured and organised. For example, services provision might be designed in fragmented fashion.
3. There is an increased demand for an integrated management of multiple chronic diseases in general practice.

Study setting and participant selection

NCD programme leaders in the health system, including the Federal Ministry of Health (FMoH) and Regional Health Bureau (RHB), and service providers including medical doctors and nurses will be purposively recruited for the case study. Patients with multimorbidity will also be purposively selected (based on information richness as suggested by the service providers) and interviewed by using a semistructured interview guide about how they are being approached and managed. Patients involved in the quantitative study will not be included in the qualitative study.

Sample size

One NCD programme leader will be approached at both FMoH and RHB levels. Two medical doctors and two nurses will be purposively selected from each participating facility for the in-depth interview. More participants may be enrolled depending on the extent of data saturation. With regard to recruitment of patients, we aimed to enrol a minimum of 16 patients with different age, sex, socioeconomic status, multimorbidity patterns and facility type. However, more patients will be involved until point of data saturation is achieved.

Data collection

A semistructured topic guide will be used to conduct the in-depth interview with programme leaders and care providers. Desk review of relevant documents (policies, strategic directives, treatment protocols and guidelines) will also be made at all levels. The PI and experts in qualitative research will collect the qualitative data.

Service providers (doctors, nurses) will be asked about how they understand (current state of knowledge) and manage NCD multimorbidity. Data collectors will also explore how services are arranged and whether staff are trained. Availability of guidelines and essential technologies for detection, diagnosis and monitoring of patients and availability of drugs and infrastructure needed for NCD multimorbidity care provision will also be explored. Patients will also be interviewed to triangulate the findings.

Patient perspectives such as their lived experience, experience of care, perceived quality of care, challenges

in the continuity of care and satisfaction with the care will be explored and audio recorded. Interviews will be carried out until saturation of data is achieved.⁸²

Field notes will be recorded during and after each interview, including descriptions of where the interview was held, reflections on how the interview went to get a deeper understanding of what was going on and what patients are describing.

Data analysis

The data from the interviews will be transcribed verbatim into Amharic by the qualitative data collectors together. Transcripts will be verified by the PI for their accuracy by listening to the audio records and field notes will be reviewed during the transcribing process. The finalised transcripts will then be translated into English. The data will be analysed by the PI using thematic analysis.

A framework approach thematic analysis will be made using key themes based on the questions followed by an inductive analysis as themes emerge. The Open Code software will be used for the analysis to assist and to facilitate the coding processes and data reduction, and further categorisation will be done to make sense of the essential meanings of the phenomenon and to allow the emergence of the common themes. Relationship between the data collected from the different study participants will be examined and emerging themes in terms of clinical decision-making and healthcare delivery for patients with multimorbidity will be organised to investigate similarities and differences within and across participant groups. We will ensure that the data are well converged to understand the overall case through categorical aggregation. We will also involve experienced research team members in the analysis phase and ask them to provide feedback on our ability to integrate the data sources to answer the research questions.

Data quality assurance/trustworthiness

Quality of the data and trustworthiness will be improved through ensuring credibility, dependability, confirmability and transferability of the data collection and interpretation process.

Credibility

Attention to all relevant voices will be given and prolonged engagements in reading and analysing the transcribed data will be sought to gain contextual details and vividly illustrate the perception and real-world experience of leaders, care providers and clients. In addition, sensitive or differing perspectives in the study sample, negative cases and perspectives that may diverge or even clash will be documented and interpreted accordingly. Double coding with two people and comparing of the codes generated will also be done.

Dependability (reliability)

To ensure that the process of data collection is replicable and minimise subjective bias, a team of experienced qualitative researchers will collect the data from various

sources. Data collectors will employ a consistent way of exploring and documenting responses from the participants. The PI will ensure patterns of responses are consistent and stable across data sources.

Confirmability

Appropriate tools will be used to accurately document participants' perspectives and experiences. The notion of reflexivity—documenting data collectors' role in the research process, such as own assumptions and biases during data collection and interpretation, will also be recorded. Moreover, an audit trail—documenting notes and other field materials developed, collected and stored along the process of data collection, analysis, interpretation and conclusion, will be considered for future verification. The extent that the findings extracted from the data reflect local, 'on-the-ground' realities and are not influenced by our own predisposed ideas will be explained as well.

Transferability

We will provide a rich and thick description of the research process and findings, including research context, characteristics of the study participants, the nature of their interactions with the researcher and the physical environment that others may decide how transferable the findings are to other contexts.

Patient and public involvement

No patient or public has been involved while developing this study protocol.

Data statement

The data to be collected in this study will be published in appropriate data repositories.

ETHICS AND DISSEMINATION

Permission to conduct the study has been obtained from the Institutional Review Board of the College of Medicine and Health Sciences, Bahir Dar University (protocol number 003/2021). Study participants will be enrolled after explaining to them the details of the objectives of the study. Only those subjects who will volunteer to participate in the study will be included after providing written consent. Permission will be sought from health facilities to be involved. Moreover, strict confidentiality of any information related to patient conditions will be maintained. To ensure this, information will be identified using codes and patient's name will not be used. Findings will be disseminated through publications in peer-reviewed journals and conference presentations.

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