Complexity in the prevention & control of non-communicable diseases (NCDs):
A latent class analysis of multimorbidity in the Jamaican Population

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Complexity in the Prevention & Control of Non-Communicable Diseases (NCDs): A Latent Class Analysis of Multimorbidity in the Jamaica population

Dissertation
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ABSTRACT (300 words)

The single-disease paradigm may not accurately reflect the individual experience, with evidence of increasing prevalence of chronic disease multimorbidity along with its heightened attendant risk of adverse health outcomes, including increased mortality. Despite high prevalence of individual non-communicable diseases within the Caribbean, exploration of the social epidemiology of multimorbidity remains sparse. This dissertation aims to (1) identify latent classes of multimorbidity in the Jamaican population; (2) estimate the association between individual-level social determinants of health and class membership; and (3) examine whether multimorbidity classes differentially impact health-related quality of life (HRQoL).

Latent class analysis (LCA) was used to examine multimorbidity patterns in a sample of 2,551 respondents aged 15-74 years and estimate associations between multimorbidity classes and HRQoL, using data from the nationally representative Jamaica Health and Lifestyle Survey 2007/2008. Analyses were based on self-reported presence/absence of 11 chronic conditions.

Approximately one-quarter of the sample (24.05%) were multimorbid, with significantly higher burden in females compared to males (31.58% vs. 16.11%; $p<0.001$). LCA revealed four distinct profiles: a *Relatively Healthy* class (52.70%), with a single or no morbidity; and three additional classes, characterized by varying degrees and patterns of multimorbidity, labelled *Metabolic* (30.88%), *Vascular-Inflammatory* (12.21%), and *Respiratory* (4.20%). Advancing age ($p<0.001$) and recent healthcare visits ($p<0.001$) were associated with multimorbidity patterns overall. Insurance ownership (RR=0.63; $p<0.01$) and higher educational attainment (RR=0.73; $p<0.05$) were associated with lower relative risk of belonging to the *Metabolic* class while female sex independently predicted membership in the *Vascular-Inflammatory* class (RR=2.54; $p<0.001$). Class membership differentially predicted HRQoL outcomes related to both physical and mental dimensions.

Results of this dissertation provide a nuanced understanding of the prevalence and social patterning of multimorbidity in Jamaica and demonstrate the clinical utility and predictive validity of multimorbidity latent classes, with potential to inform screening programs, health system reforms and intervention planning.

For Mum, Dad, Ricky and Gramps

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MULTIMORBIDITY PREVALENCE AND PATTERNS IN JAMAICA: A LATENT CLASS ANALYSIS

ABSTRACT (300 words)

Background: Evidence suggests that the single-disease paradigm does not accurately reflect the individual experience, with increasing prevalence of chronic disease multimorbidity, in addition to subtle yet important differences in the types of co-occurring diseases. Knowledge of multimorbidity patterns can aid clarification of individual-level burden and needs, to inform prevention and treatment strategies.

Objectives: To determine the prevalence of multimorbidity in Jamaica, identify subgroups of the population with similar and distinct disease profiles, and examine consistency in patterns across statistical techniques.

Design and Methods: Latent class analysis (LCA) was used to examine multimorbidity patterns in a sample of 2,551 respondents aged 15-74 years, based on data from the nationally representative Jamaica Health and Lifestyle Survey 2007/2008 and self-reported presence/absence of 11 chronic conditions. Secondary analyses compared results with patterns identified using exploratory factor analysis (EFA).

Results: Nearly one-quarter of the sample (24.05%) were multimorbid (i.e. had ≥2 diseases), with significantly higher burden in females compared to males (females:31.58% vs. males:16.11%; $p<0.001$). LCA revealed 4 distinct classes, including a predominant *Relatively Healthy* class, comprising 52.70% of the sample, with little to no morbidity. The remaining 3 classes were characterized by varying degrees and patterns of multimorbidity and labelled *Metabolic* (30.88%), *Vascular-Inflammatory* (12.21%), and *Respiratory* (4.20%). The four diseases determined using physical assessments (obesity, hypertension, diabetes, hypercholesterolemia) were primary contributors to multimorbidity patterns overall. EFA identified 3 patterns described as "Vascular" (hypertension, obesity, hypercholesterolemia, diabetes mellitus, stroke); "Respiratory" (asthma, COPD); and "Cardio-Mental-Articular" (cardiovascular disease, arthritis, mental disorders).

Conclusion: Findings revealed a high burden of multimorbidity in the Jamaican population, that is predominantly borne by females. Consistency across methods supports the validity of patterns identified and the non-random association of diseases. Future research into the causes and consequences of multimorbidity patterns can guide development of strategies that allow for more targeted prevention and intervention.

Introduction

Morbidity describes the departure from a state of physical or psychological well-being as a result of disease.[1] Today, non-communicable diseases (NCDs) have been established as the primary cause of morbidity, with a considerable attendant premature mortality burden that disproportionately impacts poor, vulnerable and socio-economically disadvantaged populations within low -and middle- income countries (LMICs).[2–4] Adding to the social, financial and physical burdens associated with management of NCDs, is the predominant single-morbidity approach of clinical care guidelines, despite evidence that these diseases seldom occur in isolation, with an increasing proportion of persons experiencing multiple coexisting chronic diseases or multimorbidity.[5–9]

Defined as the co-occurrence of two or more diseases in a given person, multimorbidity is not the same in every case, with evidence across settings suggestive of important differences with regard to the type, prevalence and distribution of co-occurring conditions across populations.[5–15] Notably, this evidence has largely originated from high-income settings throughout Europe, North America, Canada and Australia, with a large and nationally representative Scottish study demonstrating that, across 40 chronic conditions, there were more people with multimorbidity than a single disease alone.[9] One multi-country study – using data on a cross-sectional sample of adults older than 50 years from the Collaborative Research on Ageing in Europe (COURAGE) project (in Finland, Poland, and Spain) as well as the World Health Organization (WHO) Study on Global Ageing and Adult Health (SAGE) survey (in China, Ghana, India, Mexico, Russia, and South Africa) – provides insight into global multimorbidity patterns, identifying hypertension, cataract and arthritis as the most prevalent comorbid conditions, and noting that multimorbidity across low-, middle- and high-income countries generally consists of "cardio-respiratory" (angina, asthma, and chronic obstructive pulmonary disease), "metabolic" (diabetes, obesity, and hypertension), and "mental-articular" (arthritis and depression) patterns.[14]

Although a growing body of literature has been attempting to describe patterns and clusters of diseases, multimorbidity remains a complex phenomenon, with a vast variety of potential disease combinations that make it difficult to analyse.[11] Furthermore, in the absence of an established "gold standard" for multimorbidity measurement, considerable variation exists in the application of statistical methods to studies of this phenomenon.[5,11,12,16] Indeed, recent systematic reviews caution that substantial methodological heterogeneity precludes making effective comparisons of multimorbidity prevalence across available studies, citing challenges such as differences in sample sizes, age and recruitment of study participants, data sources used, number and type of baseline disease considered, and statistical procedures applied.[5,8,16] With regard to statistical methods, previous studies have typically relied on simple disease counts to specify whether a person has two or more conditions from a pre-defined list.[5,16–18] More recently, exploratory factor analysis (EFA) and traditional cluster analysis techniques have emerged as commonly used methods[8], with latent class analysis (LCA) being increasingly applied to studies of multimorbidity patterns.[11–13,19–22] Despite recognized – and increasing – methodological diversity, however, few studies have endeavoured to increase the reliability of findings through comparison of statistical techniques. To date, only two multimorbidity studies have examined the use of different analytic approaches. One study of 408, 994 patients aged 45-64 years in Catalonia, Spain used data from electronic health records to compare patterns identified via hierarchical cluster analysis and EFA methods.[23] Diagnoses were extracted using 263 blocks (disease categories) of the International Classification of Diseases version 10 (ICD-10), with authors concluding that while disease groupings from the two analytic methods did not always match exactly, there was some consistency in multimorbidity patterns.[23] The other study was conducted among a cross-sectional sample of 4,574 Australian adults, 50 years of age and older, based on self-reported presence/absence of 10 NCDs.[12] Study investigators compared multimorbidity patterns identified via commonly occurring pairs and triplets of comorbid diseases, cluster analysis of diseases, principal component analysis and LCA, finding consistency in results across methods that is suggestive of the co-occurrence of diseases beyond chance.[12] Both studies emphasized the need to strengthen the evidence base on multimorbidity prevalence and patterns, to better inform disease management and healthcare delivery.[12,23]

In a similar vein, current literature consistently notes that efforts to prevent and control the rising NCD burden require increased attention to the complex needs of a growing population with chronic disease multimorbidity.[5,8,17,24–26] International organizations, such as WHO, the European Forum for Primary Care and the National Institute for Health and Clinical Excellence (NICE) , all echo this sentiment noting that knowledge of associations beyond chance (i.e. identification of patterns of multimorbidity) in a given population is an important first step towards generating an evidence base for actual clinical practice, with significant implications for patient-oriented prevention, diagnosis, treatment, and prognosis.[8,27,28]

Rationale & Purpose

Throughout WHO regions worldwide, the burden of NCDs is purportedly highest in the Americas, with higher rates among peoples in the English-speaking Caribbean nations.[3,29,30] Within this Caribbean community, Jamaica has been conducting epidemiological studies over the past several decades to gather information on public health challenges, risk factors and behavioural practices associated with NCDs.[31–33] Consequently, ample research on the prevalence of NCDs has been conducted in Jamaica, including comprehensive national health surveys such as the Jamaica Health and Lifestyle Surveys 2000/2001 (JHLS-I) and 2007/2008 (JHLS-II).[32,34–36] These studies provide a well-established evidence base of a severe NCD burden that is predominantly borne by females.[32–36] Specifically the latest JHLS-II survey reported prevalence estimates of 25% (25.5% females; 25.0% males), 8% (9.3% females; 6.4% males), 12% (15.6% females; 7.5% males), 27% (27.1% females; 26.0% males) and 25% (37.5% females; 12.3% males) for hypertension, diabetes, hypercholesterolemia, overweight and obesity, respectively.[33,34] Further, estimates from the JHLS-II indicate that overweight/obesity doubles the odds of hypertension, diabetes mellitus and high cholesterol in males and triples the odds of having high cholesterol and hypertension among females.[32] Amongst those with NCDs, studies in Jamaica also suggest that depressive symptoms and greater dissatisfaction with life are often reported, with greater frequency in females than males.[32,33] Together, this evidence not only suggests an expanded burden of NCDs (i.e. an increased likelihood that individuals are suffering from multiple co-occurring chronic conditions), but the gender discrepancy further implies that multimorbidity profiles may be different among men and women. However, no investigation of multimorbidity prevalence or patterns has yet been undertaken for Jamaica, or the larger Caribbean region.

The first paper of this dissertation research aims to address this research gap via secondary analysis of the 2007/2008 JHLS-II dataset. First, LCA will be used to identify classes of individuals in the Jamaican population with distinct multimorbidity patterns and examine whether these patterns are similar across sex. Knowledge of multimorbidity prevalence and patterns can enable better appreciation of the true burden of disease, with important implications for development of strategies that aid the early identification of vulnerable populations, facilitate prevention of future health conditions and support management of existing ones.[10,37] As an additional step towards assessing the validity and reliability of multimorbidity profiles identified via LCA, EFA will also be used to compare consistency (or variation) in patterns identified across the two methods.

Research Questions and Hypotheses

This paper aims to answer the following research questions:

1. What underlying subgroups (i.e. latent classes) adequately represent the heterogeneity of multimorbidity in the Jamaica population?

a. What are the patterns of multimorbidity in this population and their corresponding prevalence?

b. Are these multimorbidity patterns similar across sex?

2. How do the identified patterns of multimorbidity compare using LCA versus EFA?

Although several hypotheses have informed this dissertation, the research remains largely hypothesis-generating (rather than hypothesis-testing), with use of an exploratory LCA technique to identify subgroups of the population with similar and distinct disease profiles. Accordingly, no *a priori* assumptions have been made regarding the number of latent classes to be identified or the underlying NCDs by which each group will be characterized. Nonetheless, given findings from research on global multimorbidity patterns, in addition to evidence of a high prevalence of hypertension, diabetes, asthma, arthritis and depression in the Jamaica population,[32–34] it is expected that NCD clusters will include similar "cardio-respiratory", "metabolic" and "mechanical/arthritic-mental" patterns. It is further expected that multimorbidity patterns will differ across sex.

Methods

Data

The JHLS-II is a nationally representative study that was coordinated at the Epidemiology Research Unit (ERU) of the Tropical Medicine Research Institute (TMRI), the University of the West Indies, Mona, recruiting a sample of 2,848 Jamaicans, 15-74 years of age over a four-month period spanning from November 2007 and March 2008, via a multi-stage cluster sampling design.[32,33] An interviewer-administered questionnaire was used to obtain data on demographic characteristics, medical history and health behaviours, including physical (i.e. height, body weight, hip circumference, waist circumference) and biological (i.e. blood pressure, blood glucose, total cholesterol) measurements that were made in accordance with standardized protocols.[32,33] Evidence of good data quality measures included low non-response rate (1.7%) and the maintenance of good inter- and intra-observer reliabilities throughout the survey.[32] Further details of the survey design, sampling procedures and data collection methods are provided in the technical report.[32]

Measures

Indicators of multimorbidity were limited to those NCDs with the greatest burden in the population (i.e. prevalence greater than or equal to 1% in each sex). Following guidance from the 2011 systematic review on multimorbidity measurement by Diederichs and colleagues that related diseases be combined,[16] cardiovascular disease (i.e. heart disease, myocardial infarction, and circulation problems) and mental health disorders (i.e. depression, anxiety, psychosis, and other mental health problems) were grouped together to enhance data quality. Self-reported diagnosis of bronchitis/pneumonia was used as a proxy indicator of chronic obstructive pulmonary disease (COPD). The final list of 11 conditions included hypertension, obesity, hypercholesterolemia, diabetes, asthma, arthritis, cardiovascular disease, mental health disorders, COPD, stroke, and glaucoma.

Presence or absence of these final 11 conditions was largely based on self-report, with the exception of four diseases (obesity; hypertension; diabetes; hypercholesterolemia) where physical assessments were available and used alone, or in combination with self-reports, to increase measurement validity and reliability. Specifically, objective measurements of height and weight were used to determine obesity status (BMI $\geq$ 30 kg/m^2), in accordance with WHO guidelines.[2] Diabetes was defined as having a fasting plasma glucose value $\geq$ 7.0 mmol/L (126 mg/dl) or being on medication for raised blood glucose.[2] Hypertension was defined as systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg or using medication to lower blood pressure.[2] Hypercholesterolemia was defined as total cholesterol levels of 5.2 mmol/l or higher or self-reported use of medications to control blood cholesterol.[2]

Multimorbidity was defined as having two or more of the final list of 11 NCDs. A 2012 systematic review by Fortin and colleagues advised inclusion of at least 2 operational definitions of multimorbidity: (1) the presence of two or more diseases; and (2) the presence of three or more diseases; noting that the latter definition may be more meaningful for clinicians given that a simple count of 2 or more diseases is less discriminating.[5] Accordingly, descriptive analyses also use the latter definition to allow for identification of individuals with higher needs and greater disease burden.[5]

Statistical Approach

Analyses were restricted to participants with non-missing information on the 11 NCD multimorbidity indicators. Of the 2,848 respondents who completed the survey, 311 (10.9%) were missing information on one or more of these indicators. There were no statistically significant differences between those with complete and those with missing information on the basis on sex, age or region of residence. The final analytic sample of 2,551 respondents included 790 males and 1,761 females.

Descriptive statistics were calculated for the overall sample and each sex group, to determine the prevalence of morbidity (from individual NCDs) and multimorbidity. Means with 95% confidence intervals (for continuous variables), and proportions (for categorial variables) were computed and compared using the Mann-Whitney U test and the Pearson χ^2 statistic, respectively, to examine differences across sex. All analyses were weighted to account for sampling design and non-response as well as differences in the age-sex distribution of the study sample compared to the Jamaican population. Base sampling weights reflected the product of the inverse of the probability of selecting a household and the inverse of the probability of selecting a primary sampling unit, adjusted for non-response. Post-stratification weights were calculated as the number of persons in the Jamaican population between the ages of 15-74 years, represented by each individual in the sample within 5-year age-sex categories.

Latent class analysis (LCA)

Identification of the baseline model

LCA was used to identify discrete, mutually exclusive classes of individuals with distinct multimorbidity patterns, based on the presence or absence of the final list of 11 NCD indicators (i.e. hypertension, obesity, hypercholesterolemia, diabetes, asthma, arthritis, cardiovascular disease, mental health disorders, COPD, stroke, and glaucoma). LCA models define class membership based on the probabilities of the observed values of all indicators for the individuals (Figure 1).[38,39] LCA therefore permits different subgroups of respondents with differing disease profiles to be determined probabilistically based on their responses to questions about the presence of specific NCDs.[38,39]

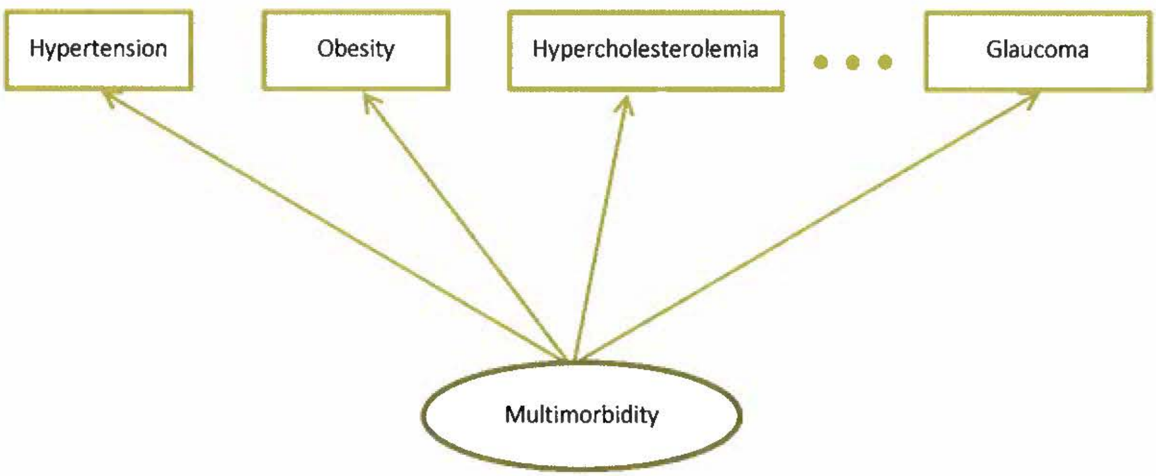

Figure 1. Latent class model of multimorbidity

In order to identify an optimal baseline model, a sequence of LCA models was examined beginning with a single-class model and adding classes in a stepwise fashion until model fit no longer significantly improved. Models with 1 through 6 classes were fit to the data, with final model selection based on a balance of parsimony, substantive consideration (i.e. the meaningfulness and distinctiveness) of each model and comparison of a range of model fit indices. To ensure that the global maximum (rather than local maximum) was identified, an iterative maximum likelihood estimate was used, with a minimum of 200 'random' sets of starting values.[38,39] The number of random sets was increased as needed to achieve model identification. Models that are identified have one dominant solution that is arrived at most frequently among various sets of starting values (i.e. the log-likelihood and parameter estimates are replicated).[38,39]

Several indices were used to guide model selection, including the likelihood-ratio G^2 statistic, the Akaike Information Criteria (AIC), the Bayesian Information Criteria (BIC) and the adjusted BIC.[39,40] The G^2 likelihood-ratio chi-square statistic is a common measure of absolute model fit while the AIC, BIC and the adjusted BIC are used to compare the relative fit of competing models (e.g. models with different numbers of latent classes).[38,39] The likelihood-ratio G^2 statistic (with corresponding degrees of freedom and p-values) tests the null hypothesis that the specified LCA model fits the data (i.e. a significant p-value indicates lack of model fit in absolute terms).[38,39] Given somewhat small sample size relative to the number of potential disease combinations, however, there was a concern that absolute fit of the model would be difficult to test due to sparseness.[41] When sparseness is an issue, the distribution of the G^2 statistic is not well approximated by the chi-square.[41] To obtain a reference distribution for the G^2 statistic, despite the relatively large degrees of freedom, the parametric bootstrap approach was applied.[41,42] In the parametric bootstrap, many random datasets are generated based on the parameters estimated from the empirical data, the model is fit to each random data set and the test statistic computed, and then the resulting distribution of the test statistic across the random data sets is used as the reference distribution.[41] A significant *p*-value on the parametric bootstrap likelihood ratio test indicates that the null model is too restrictive.

With the information criteria, on the other hand, lower values suggest a more optimal balance between model fit and parsimony.[38,39] Notably, studies have suggested that when the true number of classes is large and the sample size small, the BIC seriously underfits.[43] Furthermore, evidence from simulation studies of LCA models have indicated that the adjusted BIC generally performs better than other information criteria, particularly with smaller samples and more unequal class sizes.[43,44] Thus, while values for all information criteria were considered, the adjusted BIC and AIC were given greater weight.

Finally, probability plots for the latent classes were inspected to consider the substantive interpretability of the resultant latent class solutions, with model interpretability assessed using the following criteria: (1) classes were easily distinguished from each other based on item-response probabilities; (2) classes were not trivial in size (i.e. no class has a near-zero probability of membership); and (3) there was potential to assign a meaningful label to each class.[39] The prevalence of each latent class was calculated as the average across participant-specific class membership probabilities.[39] Once the baseline model had been selected, participants were assigned to one class based on their maximum posterior probability and the mean posterior probability of each latent class determined.[41] Mean posterior probabilities above 70% indicate optimal fit.[21]

Given the potential for obesity to have a double impact, as a *risk factor* for individual NCDs and as a *disease* requiring intervention, sensitivity analyses explored patterns of multimorbidity based on only 10 NCD indicators (i.e. excluding obesity).

Testing measurement invariance across sex

Following guidelines by Lanza et al (2007) which recommend that analyses begin by fitting a baseline model with no grouping variable or covariates, sex was added as a grouping variable after the baseline model had been selected, to test the hypothesis that multimorbidity patterns vary across sex. To test measurement invariance empirically, the model was run with all parameters freely estimated and again with item-response probabilities constrained equal across groups. The difference in the G^2 statistic between the two models was compared to the chi-square distribution for the difference in the models' degrees of freedom, and a significant p-value indicative of different measurement across groups.[38,39]

Exploratory factor analysis (EFA)

EFA was used to identify the underlying factors that summarized the correlation between the NCD indicators (i.e. multimorbidity patterns) and compare similarities and/or differences between this statistical technique and LCA results. In accordance with the definition of multimorbidity as two or more diseases, an identified factor needed consist of at least two diseases to qualify as a multimorbidity pattern.

Based on examples used in previous studies,[7,15] along with the recommendations from systematic reviews,[5,16] the following criteria were applied during EFA: only those NCDs with a prevalence ≥ 1% in each sex were included; data on NCDs were coded in binary form and tetra-choric correlation matrices[a] used owing to the dichotomous nature of the NCD variables; and the principal components extraction method applied. The principal components extraction method allowed for determination of the number

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[a] Previous multimorbidity research notes that although disease morbidity is generally coded in binary format (i.e. 0= has disease; 1= does not have disease), statistical packages for performing EFA often require data to be in a continuous format. These sources note, however, that this challenge can be overcome by using the tetrachoric technique to estimate the correlation between two theorised continuous variables, from two observed ordinal ones.[18]

of factors to use, in combination with eigenvalues > 1 and scree plots to visually assess importance and narrow down the selection of factors. Finally, the oblique rotation method was applied to evaluate the factor solution and facilitate interpretation of factor loadings. Oblique rotation was used owing to correlations between NCDs. Factor loadings > 0.30 were taken as the minimum acceptable value for a significant correlation in the identification of diseases comprising each multimorbidity pattern. The Kaiser-Meyer-Olkin (KMO) statistic was used as a measure of sample adequacy.[7,15,45]

All statistical analyses were carried out via Stata v.15 software, using the LCA Stata Plugin[46] and the LCA Bootstrap Stata macro[42] as needed, with statistical significance indicated by a p-value < 0.05.

Results

Sample description

Of the 11 NCD indicators included in the LCA, two diseases had an overall prevalence of about 25.00%, four had a prevalence between 5.00% - 12.00%, while the remaining five had lower prevalence, typically under 5.00% (Table 1; Figure A1).

Among this sample of the Jamaican population, hypertension was most prevalent NCD (25.33%), followed by obesity (25.23%), hypercholesterolemia (11.53%), diabetes (7.86%) and asthma (6.85%). About one third (30.57%) of the sample reported only one NCD while nearly one-quarter (24.05%) reported multimorbidity (i.e. two or more diseases). When the more discriminating definition of multimorbidity was applied, approximately 1 in every 10 participants (10.16%) reported at least 3 NCDs.

Table 1. Prevalence of Select Non-Communicable Diseases (NCDs) by sex (JHLS-II data, 2007/2008; N=2,551)				
	Males (n=790)	Females (n=1,761)	Total (N=2,551)	*p*-value
Mean age (95% CI), years	37.04 (36.60, 37.48)	36.93 (36.64, 37.22)	36.98 (36.70, 37.27)	0.649
NCD Prevalence				
Hypertension	25.48	25.18	25.33	0.848
Obesity	11.97	37.80	25.23	**<0.001**
Hypercholesterolemia	7.53	15.33	11.53	**<0.001**
Diabetes mellitus	6.46	9.19	7.86	**0.020**
Asthma	5.67	7.97	6.85	0.068
Arthritis	2.10	8.22	5.24	**<0.001**
Cardiovascular disease	2.40	6.72	4.62	**<0.001**
Mental health disorders	2.63	3.28	2.96	0.409
COPD	2.08	3.49	2.80	0.176
Stroke	1.23	1.20	1.21	0.946
Glaucoma	1.08	1.13	1.10	0.879
Multimorbidity (2+ NCDs)	16.11	31.58	24.05	**<0.001**
Multimorbidity (3+ NCDs)	5.34	14.73	10.16	**<0.001**
Mean number of NCDs reported (95% CI)	0.69 (0.63, 0.74)	1.19 (1.14, 1.25)	0.95 (0.90, 0.99)	**<0.001**

COPD = chronic obstructive pulmonary disease

Note: Values are weighted proportions or mean (95% CI)

p-value for difference between males and females based on chi-squared (χ^2) test or and Mann-Whitney U test, as appropriate

The multimorbidity burden was significantly greater in females (p<0.001), regardless of which definition was used. Further, there were statistically significant sex differences in the prevalence of obesity (females:37.80% vs. males:11.97%; p<0.001), hypercholesterolemia (females:15.33% vs. males:7.53%; p<0.001), diabetes mellitus (females:9.19% vs. males:6.46%; p<0.05), arthritis (females:8.22% vs. males:2.10%; p<0.001), and cardiovascular disease (females:6.72% vs. males:2.40%; p<0.001), with the burden in females often 2 to 3 times as high as that in males. On average, females reported 1.19 NCDs (95% CI: 1.14 – 1.25) while males reported 0.69 diseases (95% CI: 0.63 – 0.74) (p<0.001).

LCA results (and baseline model)

The LCA model fit results are summarized in Table 2.

Table 2. Summary of Information for Selecting Number of Latent Classes of NCD Multimorbidity (JHLS-II data, 2007/2008; N=2,551)

Number of Latent Classes	G^2	*df*	AIC	BIC	Adjusted BIC	log-likelihood	Entropy
1	1318.43	2036	1340.43	1404.71	1369.76	-8186.47	1.00
2	597.77	2024	643.77	778.19	705.11	-7826.14	0.65
3	524.61	2012	594.61	799.16	687.96	-7789.56	0.54
4	467.03	2000	561.03	835.71	686.38	-7760.77	0.58
5	Not well identified						
6	Not well identified						

NCD = non-communicable disease; df = degrees of freedom; AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion

The G^2 statistic, AIC and adjusted BIC consistently decreased up until the four-class model while the BIC reached a minimum in the two-class model. Neither models with five nor six classes were well identified – this means that even after increasing the random starts so that the estimation procedure went through a maximum set of 400 iterations, neither model converged on the same solution the majority of the time. Notably, while the adjusted BIC indicated that the 4-class model was the best fit model, it suggested relatively little difference between this and the three-class model (adjusted BIC_{4class}= 686.38 vs. adjusted BIC_{4class}= 687.96; difference = 1.58). Nonetheless, the four-class model was better identified than the three-class model, with the maximum likelihood estimate converging on the same solution 97.50% of the time (compared to 55.00% of the time for the three-class solution). The four-class solution's entropy score (0.58) indicated greater precision in class prediction (compared to the three-class solution) and, upon examination, allowed for meaningful interpretation of latent classes. Results of the parametric bootstrap likelihood ratio tests (Table 3) further supported this decision, finding statistically significant differences for all except the four-class null model and the alternative five-class model (p=0.33), indicating that the four-class model was the optimum baseline model.

Table 3. Model comparison for Selecting the Number of Latent Classes of NCD Multimorbidity (JHLS-II data, 2007/2008; N=2,551)			
Null model	**vs.**	**Alternative model**	***p*-value**
1-class		2-class	0.01
2-class		3-class	0.01
3-class		4-class	0.01
4-class		5-class	0.33

NCD = non-communicable disease

Latent class prevalences and item-response probabilities (i.e. the estimated probability of reporting particular NCD, given membership in a particular latent class) for the four-class model are graphed in Figure 2.

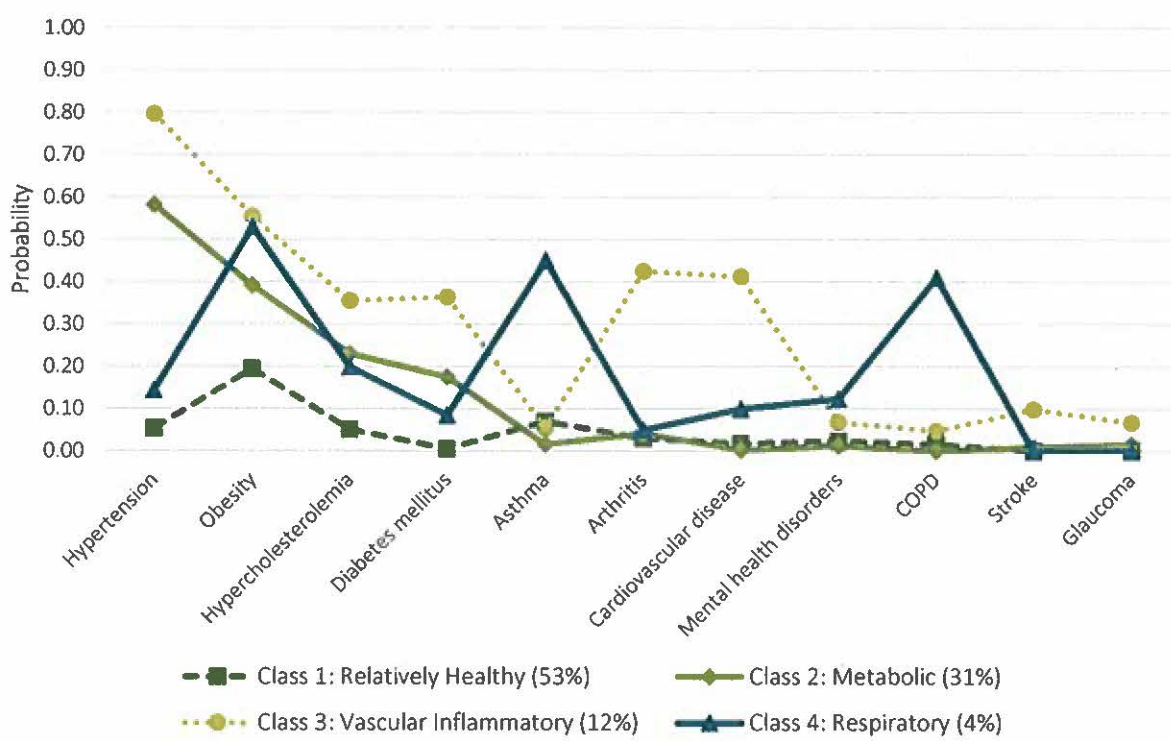

Figure 2. Item-response probabilities for the four-class model (JHLS-II data, 2007/2008; N=2,551)

Class 1 was labelled *Relatively Healthy* as it was characterized by individuals with low probabilities of all 11 NCDs (Table A1). The majority of sample respondents (52.70%) were classified into this relatively healthy class. The prevalence of multimorbidity in the *Relatively Healthy* class was 4.66% and the mean number of NCDs was 0.40. *Class 2* was characterized by individuals with a high probability of hypertension and obesity, and somewhat moderate probability of hypercholesterolemia. This class was labelled *Metabolic* and comprised 30.88% of the sample. The prevalence of multimorbidity in this *Metabolic* class was 63.60% and the mean number of NCDs was 1.60. Approximately one in five (19.80%) participants in this class had at least three NCDs. *Class 3* was characterized by individuals with a very high probability of hypertension, obesity, hypercholesteremia and diabetes. Specifically, members of Class 3 had a higher probability of these four NCDs than all other classes. Class 3 was also marked by an increased likelihood of arthritis and cardiovascular disease. This class was labelled *Vascular-Inflammatory* and comprised 12.21% of the sample. The prevalence of multimorbidity in this *Vascular-Inflammatory* class was 100% and the mean number of NCDs was 3.40. The final class, *Class 4,* was characterized by individuals with the highest probability of asthma and COPD and was accordingly labelled *Respiratory*. This was the smallest of all classes, comprising 4.20% of the sample. The prevalence of multimorbidity in this *Respiratory* class was 100% and the mean number of NCDs was 2.86.

The mean posterior probabilities for all four classes exceeded 0.70 (0.81 for the "Relatively Healthy" class; 0.75 for the "Metabolic" class; 0.86 for the "Vascular-Inflammatory" class; and 0.76 for the "Respiratory" class) suggesting optimal classification.

Sensitivity analyses exploring multimorbidity patterns using only 10 NCDs (i.e. excluding obesity), corroborated findings from the original baseline model with 11 NCD indicators (i.e. with obesity included). Specifically, LCA model fit statistics and results of the parametric bootstrap likelihood ratio test (Table A2) all pointed to the 4-class model as the optimal baseline solution. Further, results of the four-class solution suggested that the latent classes were similarly characterized as *Relatively Healthy*, *Metabolic*, *Vascular-*

Inflammatory and *Respiratory* based on the item-response probabilities; although a larger proportion of the sample was classified as being *Relatively Healthy* and smaller proportion classified as having multimorbidity (Figure A2). Under this model, individuals in the *Relatively Healthy* class were characterized by an almost negligible probability of reporting any NCD; the *Metabolic* class was characterized by individuals with a high probability of reporting hypertension and a somewhat moderate probability of reporting hypercholesterolemia and diabetes; the *Vascular-Inflammatory* class was characterized by individuals with a high probability of hypertension, hypercholesterolemia, diabetes, arthritis and cardiovascular disease; and, the *Respiratory* class was characterized by persons with a high likelihood of self-reporting asthma and COPD.

Measurement invariance

To test measurement invariance across sex, the four-class solution was estimated, first using a model with all parameters free to vary across groups and, second, in a model with the item-response probabilities constrained equal across groups (Table 4).

Table 4. Fit Statistics for Test of Measurement Invariance across Genders for NCD Multimorbidity (JHLS-II data, 2007/2008; N=2,551)

	G^2	*df*	AIC	BIC	Adjusted BIC	log-likelihood
Model 1: Item-response probabilities free to vary across genders	595.14	4001	783.14	1332.50	1033.83	-7580.69
Model 2: Item-response probabilities constrained equal across genders	725.74	4045	825.74	1117.95	959.09	-7645.99

$G^2(_2) - G^2(_1) = 130.60$, df = 44, $p < 0.01$

NCD = non-communicable disease; df = degrees of freedom; AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion

The G^2 difference test was significant ($G^2(_2)$ - $G^2(_1)$ = 130.60, df = 44, p <0.01), suggesting that measurement invariance across sex did not hold and that the two groups should be modelled separately. Accordingly, a series of models were fit to individual male and female datasets to further investigate the source of differences, with regard to the identified four-class latent structure. Table 5 shows the model fit statistics for the male and female subsamples, separately.

Table 5. Summary of Information for Selecting the Number of Latent Classes of NCD Multimorbidity for Male and Female subsamples (JHLS-II data, 2007/2008; N=2,551)

Males only (N =790)

No. of Latent Classes	G^{2*}	*df*	AIC	BIC	Adjusted BIC	log-likelihood	Entropy
1	445.89	2036	467.89	519.28	484.35	-1952.79	1.00
2	279.32	2024	325.32	432.77	359.73	-1869.51	0.64
3	220.95	2012	290.95	454.47	343.33	-1840.33	0.75
4	187.60	2000	281.60	501.18	351.93	-1823.65	0.82
5				Not well identified			
6				Not well identified			

Females only (N =1,761)

No. of Latent Classes	G^{2*}	*df*	AIC	BIC	Adjusted BIC	log-likelihood	Entropy
1	1028.54	2036	1050.54	1110.75	1075.81	-6081.94	1.00
2	490.48	2024	536.48	662.38	589.31	-5812.91	0.64
3	441.36	2012	511.36	702.94	591.75	-5788.35	0.55
4	407.44	2000	501.44	758.70	609.39	-5771.39	0.57
5				Not well identified			
6				Not well identified			

NCD = non-communicable disease; df = degrees of freedom; AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion

For both the male and female cohort, determination of the optimum model based on information criteria was less clear. In both cases, the AIC suggested a 4-class model while the BIC suggested the 2-class model. However, for the male cohort, the adjusted BIC reached a minimum with the 3-class model while, for the female cohort, it did so with the 2-class model. Based on the AIC for each subsample, in addition to examination of the distribution of item-response probabilities across all solutions, the 4-class model appeared to provide the best interpretability in each case. Parametric bootstrap analyses further supported this conclusion indicating that, for each subsample, the alternative 5-class model performed no better than the 4-class one (p_{males}=0.38; $p_{females}$=0.35) (Table 6). The 4-class model was thus selected as the baseline model for optimal balance of model fit, parsimony and ease of interpretation.

Table 6. LCA Model comparison for Selecting the Number of Latent Classes of NCD Multimorbidity for Male and Female subsamples (JHLS-II data, 2007/2008; N=2,551)

Males only (n=790)				Females only (n=1,761)			
Null model	vs.	Alternative model	*p*-value	Null model	vs.	Alternative model	*p*-value
1-class		2-class	0.01	1-class		2-class	0.01
2-class		3-class	0.01	2-class		3-class	0.01
3-class		4-class	0.07	3-class		4-class	0.05
4-class		5-class	0.38	4-class		5-class	0.35

NCD = non-communicable disease

For both males (Figure 3) and females (Figure 4), multimorbidity patterns generally mimicked the baseline model identified for the general population with differences, however, in both the prevalence of classes as well as the NCDs likely to be reported within each class.

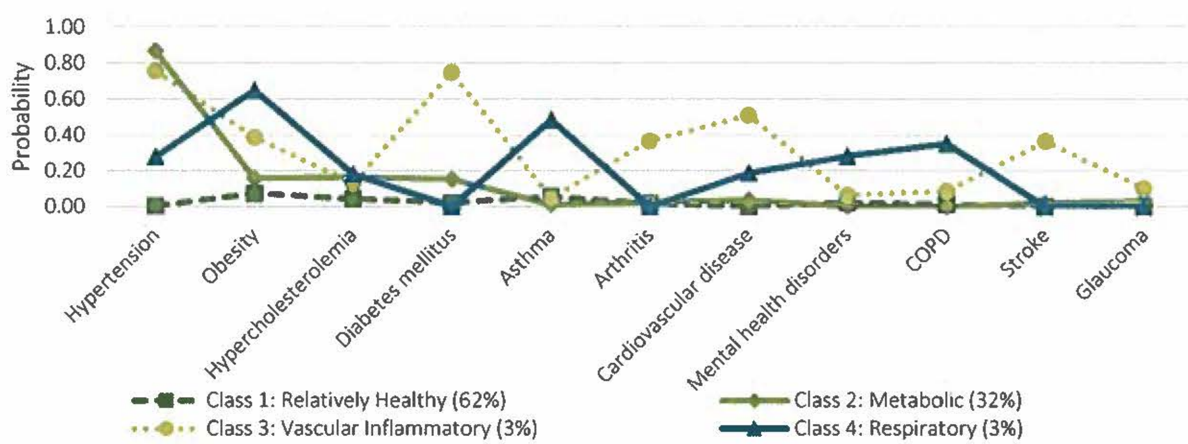

Figure 3. Item-response probabilities for the four-class model (JHLS-II data, 2007/2008; Males only: n=790)

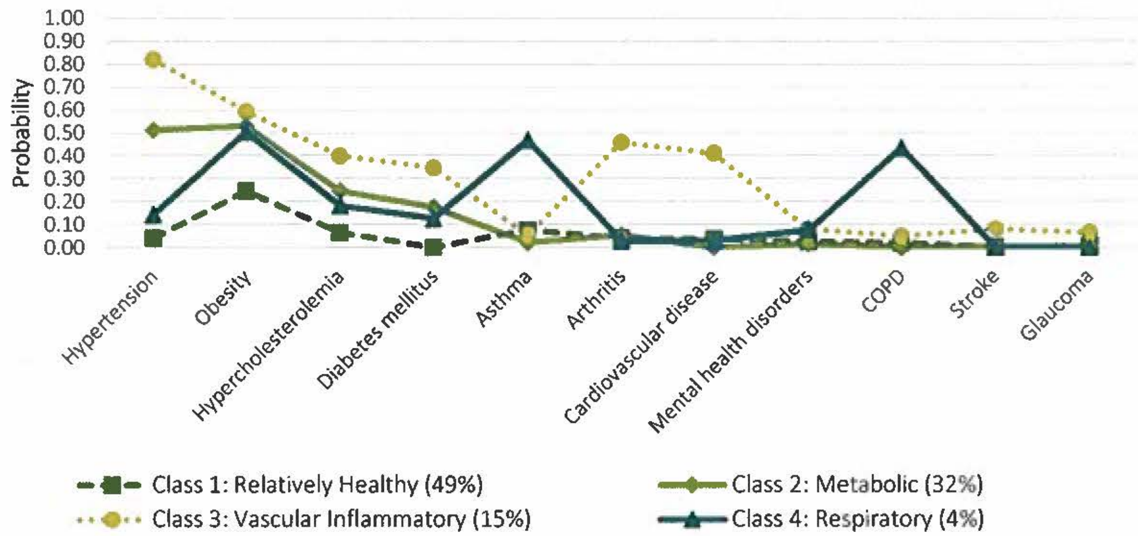

Figure 4. Item-response probabilities for the four-class model (JHLS-II data, 2007/2008; Females only: n=1,761)

Specifically, for males, the *Relatively Healthy* class comprised the majority of the sample (61.97%) and was characterized by individuals with an almost negligible probability of reporting any of the 11 NCDs. On the other hand, the *Relatively Healthy* class comprised just under half of the female sample (49.01%) and was characterized by individuals with a low probability of reporting any NCDs except obesity. The mean number of NCDs reported in this *Relatively Healthy* class was 0.28 and 0.58 for males and females, respectively (see Table A3). Almost equal proportions of the male and female subsamples (males: 32.10%; females: 31.83%) were classified into the second *Metabolic* class. Among males, however, hypertension was the only NCD of high probability while, among females, there was an increased likelihood of reporting hypertension and obesity. The prevalence of multimorbidity in the *Metabolic* class was 45.13% for males and 74.17% for females. The mean number of NCDs reported in the *Metabolic* class was 1.42 and 1.85 for males and females, respectively. Only 3.04% of the male subsample was classified into the third *Vascular-Inflammatory* class, which was characterized by an increased probability of reporting hypertension, diabetes, cardiovascular disease, obesity, arthritis and stroke. In contrast, 14.70% of the female subsample was classified into the *Vascular-Inflammatory* class, which was characterized by an increased probability of reporting hypertension, obesity, arthritis, cardiovascular disease, hypercholesterolemia and diabetes. The mean number of NCDs reported in the *Vascular-Inflammatory* class was 3.79 and 3.64 for males and females, respectively. The prevalence of multimorbidity was 100% for both males and females. The final *Respiratory class* was characterized by individuals with a high probability of reporting obesity, asthma and COPD, comprising 2.89% and 4.45% of the male and female subsamples, respectively. The prevalence of multimorbidity in this class was 100% for both males and females while the mean number of NCDs reported was 3.31and 2.65 for males and females, respectively.

EFA results

Adequacy of the sample for factor analysis was confirmed by the KMO statistic of 0.69, which exceeded the recommended value of 0.60.[47,48] Results supported evidence of three factors (i.e. multimorbidity patterns), with identification of three components with Eigenvalues greater than one. The scree plot showed the first major inflection (i.e. elbow) at the third factor, similarly suggesting retention of three factors for final analysis (Figure 5).

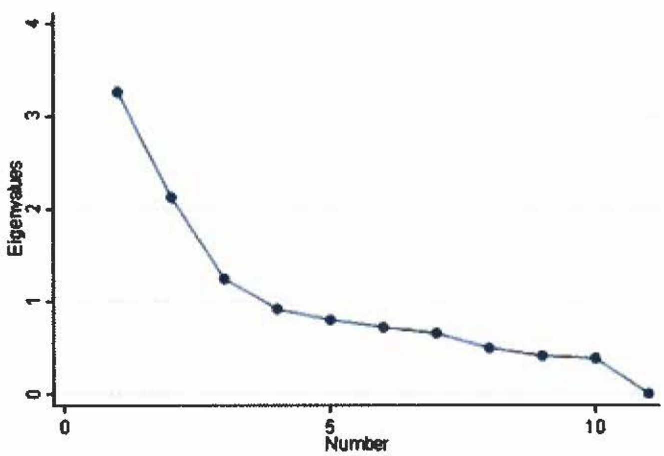

Figure 5. Scree plot of eigenvalues (JHLS-II data, 2007/2008; N=2,551)

The three-factor solution collectively explained 60.27% of the variance of the total model, with each component explaining 29.65%, 19.31% and 11.30% of the variance, respectively. Following rotation, a simpler structure was identified with strong factor loadings on each of the three components, all having absolute values above the acceptable threshold of 0.30 (Table 7). Two NCDs (arthritis and cardiovascular disease) showed strong correlations with more than one factor (i.e. multimorbidity patterns).

Table 7. Factor Scores & Pattern Matrix (JHLS-II data, 2007/2008; N=2,551)

	Factor 1: Vascular	Factor 2: Respiratory	Factor 3: Cardio-Mental-Articular
Hypertension	0.76		
Obesity	0.50		
Hypercholesterolemia	0.61		
Diabetes mellitus	0.71		
Asthma		0.34	-0.57
Arthritis		0.31	0.61
Cardiovascular disease	0.32		0.69
Mental health disorders			0.68
COPD		0.92	
Stroke	0.79		
Glaucoma		0.95	

Extraction method: Principal component analysis. Rotation method: Oblique oblimin with Kaiser normalization.

Three multimorbidity patterns were identified in the Jamaican population using EFA: "vascular" (hypertension, obesity, hypercholesterolemia, diabetes mellitus, and stroke); "respiratory" (asthma and COPD), and "cardio-mental-articular" (cardiovascular disease, arthritis, and mental health disorders).

Discussion

This study is the first to use an LCA model to examine multimorbidity prevalence and patterns in the Jamaican population. Based on data on the presence/absence of 11 NCDs, four classes were identified, including a predominant *Relatively Healthy* class comprising 52.07% of the population and characterized by minimal disease. The other three classes were characterized by high burden of multimorbidity and, based on identified patterns, were labelled *Metabolic, Vascular-Inflammatory* and *Respiratory*. The resultant classes suggested an almost quantitative dimension to multimorbidity patterns (i.e. the average number of NCDs reported was higher with progressive classes), in addition to more distinct, qualitative differences in the types of diseases comprising the patterns (e.g. *Metabolic* vs. *Respiratory* classes).

Of note, the four diseases whose presence was determined using physical assessments (obesity, hypertension, diabetes, hypercholesterolemia) were primary contributors to multimorbidity patterns, particularly the *Metabolic* and *Vascular-Inflammatory* patterns. There was also a very high likelihood of reporting obesity across all multimorbidity classes. Sensitivity analyses, demonstrating similarity across findings in models with and without obesity, not only support the patterns identified but speak to the importance of obesity in increasing vulnerability to the accumulation of multiple chronic conditions in this population. This may potentially explain the added vulnerability of women to the burden of multimorbidity, given that the prevalence of obesity among females is over 3 times as high as that in males. From a programmatic perspective, this finding also highlights the need to better target obesity, which has been identified as major public health problem throughout Jamaica, and the wider Caribbean region, especially among children where a rise in prevalence has been observed. Anecdotally, civil society organizations have been emphasizing the need for school reforms and policy initiatives (e.g. taxation on sugar-sweetened beverages) to target the high and rising prevalence of obesity among Caribbean children – and results of this analysis do suggest that adolescents are at risk for the coexistence of multiple conditions. While efforts to improve the prevention and control of NCDs need focus on addressing the complex needs of persons with multimorbidity by supporting them to manage their existing conditions and prevent the accumulation of additional ones, activities need also focus on that *Relatively Healthy* subgroup for whom the presence of obesity may predispose to a multiplicity of chronic disorders.

With regard to identified sex differences in this study population, findings suggest a similar structure in the overall patterning of multimorbidity among males and females, with some key differences in both the absolute burden of multimorbidity as well as the types of diseases comprising multimorbidity profiles in each sex. Specifically, while nearly two-thirds (61.97%) of the male sample was classified as *Relatively Healthy* with little probability of reporting any NCDs, the same was true for only about half (49.01%) of the female population. Further, while similar proportions of males and females were classified into the *Metabolic* class (~32%), in males, this class was primarily driven by high likelihood of reporting hypertension while, for females, there was a high likelihood of reporting both hypertension and obesity. In both males and females, the *Vascular-Inflammatory* class was characterized by a high probability of reporting hypertension, obesity, diabetes, arthritis and cardiovascular disease. However, the prevalence of this class was smaller among males, comprising only 3.04% of the sample, compared to females where it comprised 14.70% of the sample. Notably, however, among males, the *Vascular-Inflammatory* class was additionally characterized by a high likelihood of reporting stroke, suggesting that, despite relatively low overall prevalence of this pattern, this subgroup may be at increased risk for complications, physical impairment and functional declines. The final *Respiratory* class was similar in prevalence (males: ~3% vs. females: ~4%) and disease characterization, across both sexes.

Comparison with other studies

It is challenging to compare the results described here to findings from other studies, given differences in the number and type of disease indicators used to define multimorbidity, the types of populations sampled, and the statistical methods applied. Even among studies that have applied LCA to exploration of multimorbidity patterns, comparisons remain difficult since those studies were often limited to older population subgroups and included different disease spectra.

Among studies using LCA, results from this analysis were very similar to patterns identified in a population-based survey of Danish adults, aged 16 years and over, which identified seven classes with different disease patterns, based on 15 NCD indicators.[11] First of all, a comparable proportion of the sample ($Jamaica_{15\text{-}74\ years}$: 53% vs. $Denmark_{\geq 16\ years}$: 59%) was classified as *Relatively Healthy* with minimal probability of reporting any NCD. Secondly, the *Metabolic* class – which in the present study was essentially characterized by a high probability of hypertension and obesity – was very similar to the "Hypertension" class identified in the Danish cohort. In fact, most studies identify a metabolic-type class with increased probability of reporting some combination of hypertension, obesity, diabetes and hypercholesterolemia. This class very closely resembles the 'metabolic syndrome', which is noted to encompass a clustering of visceral obesity, dyslipidaemia, hyperglycaemia, and hypertension, and has been established as a multiplex risk factor for development of cardiovascular disease.[49,50] Next, the *Respiratory* class was similar to the "Complex Respiratory Disorders" class identified in the Danish study, where high probability of reporting asthma and COPD was also observed.[11] In other studies, however, this specific pattern did not emerge and respiratory conditions were instead noted to appear within patterns that included obesity, cardiovascular disease (i.e. angina) and arthritis.[12,13,21] Finally, the *Vascular-Inflammatory* class resembled the "Complex Cardio-metabolic Disorders" class from the Danish study, with particularly high likelihood of reporting hypertension, arthritis, heart disease, diabetes and stroke. A similar "Very Sick" class was also observed in the study of American Medicare beneficiaries, where the probability of reporting any NCD was higher than that of all other classes. While the Danish study identified three additional multimorbidity patterns, these disease profiles were likely not observed in the Jamaican sample since the presence/absence of diseases comprising these patterns (e.g. osteoporosis, slipped discs/other back injuries, migraine/recurrent headache, tinnitus, allergy) was not assessed in the JHLS-II survey.

In comparison to studies applying EFA to the exploration of multimorbidity, similarities in patterns are also observed. For example, one global study of multimorbidity patterns in adults older than 50 years, using data from nine low-, middle-, and high-income countries, similarly observed a "Metabolic" (diabetes, obesity and hypertension) pattern of relevance to eight of the countries studied (i.e. China, Finland, Ghana, India, Poland, Russia, South Africa, Spain) as well as a "Respiratory" (asthma and COPD) pattern which was only relevant to two (i.e. Finland and Russia).[14] Also similar to the *Metabolic* and *Respiratory* classes identified here, one study among 13,103 Serbian adults 20 years of age or older, identified "cardiometabolic" (i.e. hypertension, diabetes, hyperlipidemia and obesity) and "respiratory" (i.e. asthma and chronic bronchitis/emphysema) patterns among their sample.[7] Further, among a sample of 3,625 Spanish adults over 50 years of age, an "aggregated pattern" (i.e. angina, hypertension, stroke, diabetes, cataracts, edentulism, arthritis) – similar to the *Vascular-Inflammatory* class identified in this study – was observed.[51] This Spanish study identified two additional multimorbidity patterns – "cardio-respiratory" (i.e. angina, asthma, chronic lung disease) and "mental-arthritis" (i.e. arthritis, depression, anxiety)[51] – which did not correspond to any latent classes identified in the Jamaican population. Of note, the multicounty study described above similarly observed these two additional patterns, noting that the "cardio-respiratory" (i.e. angina, asthma, COPD) pattern was relevant to 7 of the countries studied (i.e. China, Ghana, India, Mexico, Poland, South Africa, Spain), while the "mental-articular" (i.e. arthritis, depression) pattern was observed in 3 (i.e. China, Ghana, India).[14] These results suggest that while clustering of diseases does exist, differences in disease segments across settings and populations require further investigation to inform knowledge of disease burden and guide strategies aimed at prevention and control.

LCA vs. EFA

In this study, results from EFA were generally consistent with findings from LCA, with some minor differences. Both techniques identified three distinct multimorbidity patterns and suggested a prominence of two specific patterns of diseases (i.e. a respiratory pattern and a vascular pattern). The main difference was that in LCA there was a *Vascular-Inflammatory* class characterized by hypertension, obesity, hypercholesterolemia, diabetes mellitus, cardiovascular disease, and arthritis while, in EFA, the "vascular" pattern also included stroke but did not include arthritis. In fact, in EFA, a "cardio-mental-articular" factor emerged which included cardiovascular disease, arthritis, and mental health disorders. This factor was similar to a "mental-articular" (arthritis and depression) pattern described in the global study of multimorbidity using EFA,[14] and further suggested that EFA results in this study were in keeping with evidence from the literature of multimorbidity patterns. Specifically, systematic reviews of multimorbidity patterns note that EFA results often consist of three common factors: (1) one factor comprising a variety of cardiovascular and metabolic conditions; (2) a second factor that includes mental health problems such as anxiety and depression; and (3) a third factor including musculoskeletal disorders and/or pain, which on occasion are associated with anxiety and depression.[8,10]

Observed differences between the EFA and LCA techniques may be attributed to the variable-centred approach of the former which is based on correlations between NCD indicators. It is noted that EFA may also be problematic for binary data, which may be grouped owing to similar distributions rather than any common underlying features.[23] Conversely, the probabilistic LCA model uses a person-centred approach and may be more useful for health care planning and development of preventative strategies by providing knowledge of the likelihood of individuals presenting with similar disease profiles. Indeed, LCA allowed for a more nuanced appreciation of two multimorbidity profiles – that is, a *Metabolic* class, with a strong likelihood of metabolic disorders only (e.g. hypertension, obesity) and another *Vascular-inflammatory* class where the probability of these two metabolic disorders was even higher and also coupled with increased likelihood of diabetes, hypercholesterolemia, arthritis and cardiovascular disease. This finding may suggest that the *Metabolic* subgroup is at risk of progression to a more severe *Vascular-Inflammatory* disease pattern where the burden of multimorbidity is higher. Although, empirical analyses indicate that those in the *Metabolic* group were significantly younger than those in the *Vascular-Inflammatory* group (mean age $_{\text{Metabolic}}$= 46.07 vs. mean age $_{\text{Vascular-Inflammatory}}$ = 56.51; $p<0.001$), such a conclusion cannot be confirmed using the current study as longitudinal data is needed to explore risk of transitioning from one class to another.

Strengths and Limitations

This is the first study to assess profiles of co-occurrence of morbidities in Jamaica, or the larger Caribbean region. Via identification of distinct combinations, rather than simple counts of diseases, this study offers a richer and more nuanced understanding of multimorbidity prevalence and patterns in Jamaica, providing insight into the nature and severity of the NCD burden. It also adds to the evidence base of the multimorbidity burden in LMICs, providing data that is more comparable for other island nations which are similarly heavily affected by NCDs.

This study used 11 dichotomous NCD indicators, yielding a total of 2,048 possible response patterns (of which only 190 were observed in the sample). Accordingly, application of the LCA model allowed for a novel approach to reducing data complexity and understanding multimorbidity patterns. Yet, there are several study limitations to consider. First, issues of sample size and differences in statistical power must be considered, particularly for LCA performed separately on male and female subgroups. The number of females included in the analysis was almost twice as large as the male subsample, making sparseness an important consideration for analyses involving the latter subgroup. Not only are identification issues more common if some groups have smaller sample sizes, but differences in latent class prevalences across groups can also lead to group differences in statistical power.[41] In addition, there is some degree of classification uncertainty in LCA and this limitation should be borne in mind in interpretation of results.[41]

Secondly, measurement of multimorbidity in this study was subject to several limitations including the self-reported evaluation of several NCDs. Although the multisource method, using both subjective self-reports and objective physical/clinical assessment, may have increased reliability in measurement of four NCDs (hypertension, obesity, hypercholesterolemia, diabetes), it does not negate the fact that accuracy in reporting of the other seven NCDs may have been affected by several factors (e.g. frequency of health service visits, knowledge of the problem, honesty).[5] Inaccurate self-reporting of prevalent mental health disorders is noted in the literature,[52] and such bias may be present in this study as a result of participants failing to disclose their conditions to interviewers or diseases being undiagnosed. In contrast to potential under-reporting of mental health conditions, diseases such as asthma tend to be more commonly diagnosed in children and youth. In addition to the bias that may result from self-report, the choice to include self-reported bronchitis/pneumonia as a proxy for COPD may not be supported by other researchers who may query inclusion of this disease type within the NCD umbrella. Finally, the study was unable to assess either disease severity or the presence/absence of pain, both of which may not only influence participant self-reports but also serve as important indicators of disease control and individual capacity.

Third, the final list of 11 conditions was based largely on convenience and limited to those NCDs identified in the JHLS-II survey questionnaire. It is indeed likely that different multimorbidity profiles may have emerged if other NCDs indicators had been used in the measurement of multimorbidity. However, in the absence of a gold standard measurement for multimorbidity, this study's adherence to recommended standards, which advise inclusion of between 11-12 most prevalent or high impact chronic diseases in a given population[5,16], is a major strength of this study. Notably, this study included all diseases specified in the recommended list, with the exception of cancer – given its lower overall prevalence in the sample population.

Fourth, while the use of population-level data in this study increased the representativeness of identified patterns, the study design which excluded age-groups older than 74 years may have introduced a selection and information bias. It is well-recognized that multimorbidity assumes greater importance with advancing age[5,8,16] and failure to examine patterns in older persons omits an important population demographic where multimorbidity may be more common, with greater implications for disease severity, management of conditions, functional status and quality of life.

Conclusion

Findings indicate that a considerable proportion of the population is managing two or more conditions, with a female preponderance in the burden and degree of multimorbidity. Consistency of multimorbidity patterns identified here with results from other international studies supports the non-random association of diseases and the need for intervention to better control and support, if not prevent, the inevitable lifelong management of multiple diseases with which many populations must contend. Future work should aim to replicate these findings in other datasets, to further support the reliability and validity of patterns identified. Longitudinal datasets would further support exploration of disease trajectories and understanding of how individuals manage multiple conditions and transition to different patterns over time. Investigation of multimorbidity burden in other LMICs is also needed to better reflect individual burden of disease as well as clinician's daily workload and experience. As future research continues to examine this multimorbidity phenomenon, exploration into the causes and consequences of NCD patterns, with attention to variation in disease profiles according to sex, age and socio-economic status, can guide the development of strategies that allow for more targeted prevention and intervention.

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Appendix

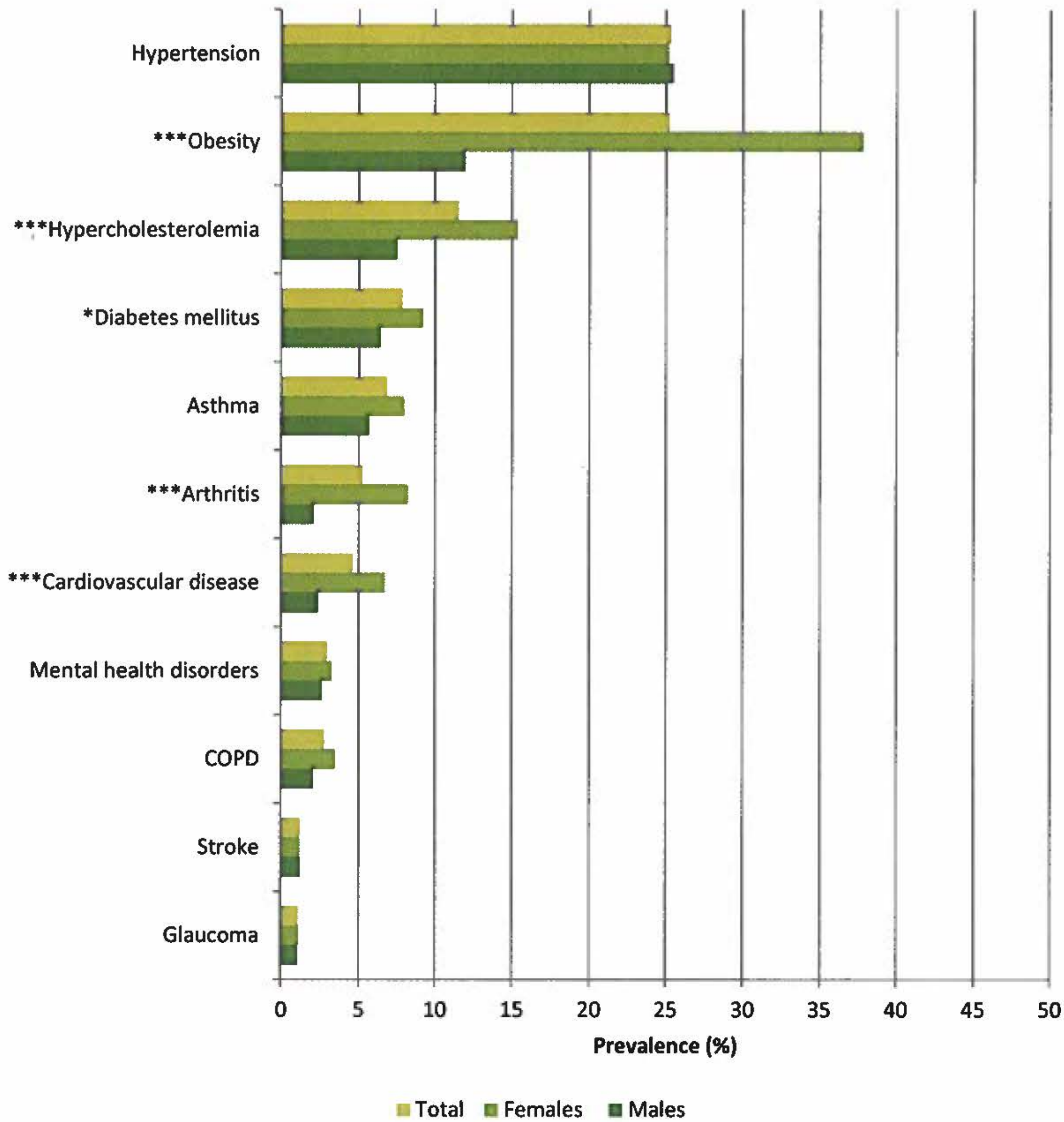

Figure A1. Prevalence of Select Non-Communicable Diseases (NCDs) by sex (JHLS-II data, 2007/2008; N=2,551)

*p<0.05, **p<0.01; *** p<0.001 (Differences for males and females)

Table A1. Four-Latent-Class Model of Multimorbidity (JHLS-II data, 2007/2008; N=2,551)				
	Latent Class			
	1	**2**	**3**	**4**
	Relatively Healthy	**Metabolic**	**Vascular Inflammatory**	**Respiratory**
Latent class prevalences	0.53	0.31	0.12	0.04
Item-response probabilities	**Probability of a Yes response**			
Hypertension	0.05	**0.58**	**0.80**	0.14
Obesity	0.20	**0.39**	**0.56**	**0.53**
Hypercholesterolemia	0.05	0.23	**0.36**	0.20
Diabetes mellitus	0.00	0.17	**0.36**	0.08
Asthma	0.07	0.02	0.06	**0.45**
Arthritis	0.03	0.04	**0.43**	0.05
Cardiovascular disease	0.02	0.00	**0.41**	0.10
Mental health disorders	0.02	0.01	0.07	0.12
COPD	0.02	0.00	0.05	**0.41**
Stroke	0.00	0.01	0.10	0.00
Glaucoma	0.00	0.02	0.07	0.00
Multimorbidity (2+ NCDs)	4.66	63.60	100.00	100.00
Multimorbidity (3+ NCDs)	0.20	19.80	84.65	59.65
Mean number of NCDs reported (95% CI)	0.40 (0.36, 0.45)	1.60 (1.53, 1.67)	3.40 (3.23, 3.56)	2.86 (2.72, 3.00)

*Item-response probabilities ≥0.35 in bold to facilitate interpretation

Table A2. Model comparison for selecting number of latent classes of multimorbidity based on 10 indicators (JHLS-II data, 2007/2008; N=2,551)†

Null model	vs	Alternative model	*p*-value
1-class		2-class	0.01
2-class		3-class	0.01
3-class		4-class	0.01
4-class		5-class	0.14

†This LCA model excludes obesity

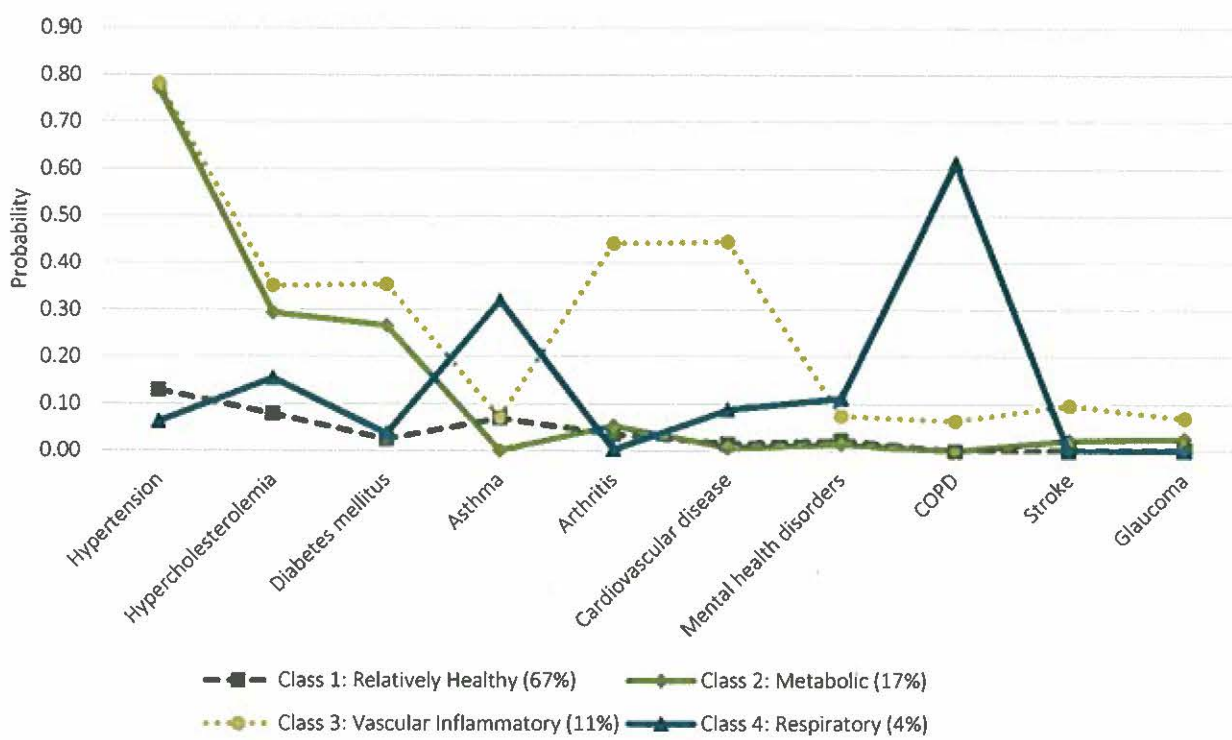

Figure A2. Probability of NCD morbidity conditional on latent class membership (JHLS-II data, 2007/2008; N=2,551)

Table A3. Four-Latent-Class Model of Multimorbidity, by sex (JHLS-II data, 2007/2008; N=2,551)

	Males (n=790)				Females (n=1,761)			
	Latent Class				Latent Class			
	1	2	3	4	1	2	3	4
	Relatively Healthy	Metabolic	Vascular Inflammatory	Respiratory	Relatively Healthy	Metabolic	Vascular Inflammatory	Respiratory
Latent class prevalences	0.62	0.32	0.03	0.03	0.49	0.32	0.15	0.04
Item-response probabilities	Probability of a Yes response				Probability of a Yes response			
Hypertension	0.01	**0.87**	**0.76**	0.28	0.04	**0.51**	**0.82**	0.15
Obesity	0.07	0.16	**0.39**	**0.65**	0.25	**0.53**	**0.60**	**0.51**
Hypercholesterolemia	0.04	0.16	0.13	0.18	0.07	0.25	**0.40**	0.18
Diabetes mellitus	0.02	0.15	**0.75**	0.00	0.00	0.18	**0.35**	0.13
Asthma	0.06	0.01	0.05	**0.49**	0.08	0.02	0.05	**0.47**
Arthritis	0.02	0.03	**0.37**	0.00	0.04	0.06	**0.46**	0.03
Cardiovascular disease	0.00	0.04	**0.51**	0.19	0.04	0.00	**0.41**	0.03
Mental health disorders	0.02	0.00	0.06	0.28	0.03	0.02	0.08	0.08
COPD	0.01	0.00	0.09	**0.35**	0.02	0.00	0.05	**0.43**
Stroke	0.00	0.02	**0.36**	0.00	0.00	0.00	0.08	0.00
Glaucoma	0.00	0.03	0.10	0.00	0.01	0.00	0.07	0.00
Multimorbidity (2+ NCDs)	3.04	45.13	100.00	100.00	6.74	74.17	100.00	100.00
Multimorbidity (3+ NCDs)	0.00	10.62	76.00	84.62	0.59	24.58	89.72	55.81
Mean number of NCDs reported (95% CI)	0.28 (0.22, 0.34)	1.42 (1.32, 1.52)	3.79 (3.39, 4.18)	3.31 (2.89, 3.72)	0.58 (0.52, 0.64)	1.85 (1.75, 1.96)	3.64 (3.37, 3.92)	2.65 (2.40, 2.90)

*Item-response probabilities ≥0.35 in bold to facilitate interpretation

SOCIAL DETERMINANTS OF MULTIMORBIDITY IN JAMAICA: APPLICATION OF LATENT CLASS ANALYSIS

ABSTRACT (300 words)

Background: Chronic disease multimorbidity is associated with impaired functioning, lower quality of life and higher mortality. While vulnerability to the accumulation of diseases may be heightened by the shared pathogenesis of many non-communicable diseases (NCDs), susceptibility is further embedded in social, economic, and cultural contexts with important differences in the prevalence, patterns and determinants of multimorbidity across settings. Despite high prevalence of individual NCDs within the Caribbean region, exploration of the social epidemiology of multimorbidity remains sparse.

Objectives: To examine the social determinants of multimorbidity in Jamaica to better inform prevention and intervention strategies.

Design and Methods: Latent class analysis (LCA) was used to examine multimorbidity patterns in a sample of 2,551 respondents aged 15-74 years and estimate the association between individual-level social determinants of health and class membership, using data from the nationally representative Jamaica Health and Lifestyle Survey 2007/2008. The analysis was based on the self-reported presence/absence of 11 chronic conditions.

Results: Approximately one-quarter of the sample (24.05%) were multimorbid. LCA revealed four distinct profiles: a *Relatively Healthy* class (52.70%), with a single or no morbidity; and three additional classes, characterized by varying degrees and patterns of multimorbidity, labelled *Metabolic* (30.88%), *Vascular-Inflammatory* (12.21%), and *Respiratory* (4.20%). Class membership was associated with advancing age ($p<0.001$) and recent healthcare visits ($p<0.001$). Further, health insurance ownership (RRR=0.63; $p<0.01$) and higher educational attainment (RRR=0.73; $p<0.05$) were associated with lower relative risk of belonging to the *Metabolic* class. Female sex independently predicted membership in the *Vascular-Inflammatory* class (RRR=2.54; $p<0.001$).

Conclusion: This study provides a nuanced understanding of the prevalence and social patterning of multimorbidity in Jamaica, with potential to inform screening programs, health system reforms and intervention planning. Future research using longitudinal designs would aid understanding of disease trajectories and clarify the role of social determinants in mitigating risk of accumulation of diseases.

Introduction

The growing NCD pandemic is spurred by common, preventable risk factors which are typically initiated during youth, continued into adulthood, exacerbated with ageing and further influenced by cultural, social, economic and environmental conditions.[1–12] This multifactorial aetiology has been described as resulting from complex interactions between individuals and their environment[1,12–15], with variation in the predisposition and occurrence of these diseases across populations.[2,16–18] Social conditions influence behavioural risk factors for NCDs (i.e. tobacco use, physical activity levels, nutrition and food consumption patterns, and harmful use of alcohol) and consequent intermediate changes in body weight and body composition (i.e. metabolic risk factors), in addition to health-seeking behaviours and opportunities to intervene in the onset, expression and outcome of disease.[1,2,10,12,13,15–17,19–24] Individually, NCDs are responsible for substantial death and disability[1,25]; importantly, when two or more NCDs occur together (i.e. multimorbidity), health outcomes are further modified, often through the decreased quality of life that results from increased burden of diseases, increased health care consumption and reduced coping strategies.[26,27]

The burden of multimorbidity has typically been studied in high-income countries, such as Europe (i.e. the Netherlands, Germany, the United Kingdom), North America (i.e. the United States, Canada) and Australia, where its prevalence and socio-economic determinants have been well established.[5,28,29] In their 2014 systematic review of the prevalence, determinants and patterns of multimorbidity in primary care, Violan and colleagues found that across 44 studies in high-income settings, all showed a significant positive association with advancing age (odds ratios [OR] ranging from 1.26 to 227.46) and lower socio-economic status (with ORs ranging from 1.20 to 1.91), with significant positive associations between female sex and mental disorders additionally observed in many sites.[28] Following this systematic review, an increasing number of studies have been conducted, particularly throughout low- and middle-income settings, to examine the relationship of specific determinants with prevalent multimorbidity and illustrate how socio-economic characteristics, lifestyle behaviours and health system factors influence the co-occurrence of multiple chronic diseases.[29–34] These studies, which were largely based on disease counts, found that multimorbidity and morbidity generally had similar determinants,[29,31–35] noting that a stronger association of age, level of education and type of health insurance with multimorbidity in comparison to morbidity was suggestive of these factors being independent determinants of the former.[29,35] Among Chinese adults, multimorbidity has been associated with increased odds of being a past or current smoker[31–33], having a salty diet preference[31], no physical activity[31] and regular use of secondary outpatient care in preference to primary care.[31] Notably, while data from high income settings has suggested that multimorbidity is associated with socio-economic deprivation,[28] evidence from low- and middle income country settings suggests an inverse relationship, with greater likelihood of reporting multimorbidity among individuals with higher per capita household income in China[31] and South Africa.[29] Together, these data suggest that while vulnerability to multimorbidity may be heightened by the common aetiology and shared pathogenesis of many NCDs, susceptibility is further embedded in social contexts and conditioned by the environment in which people live and work, their adaptive capacities and their behavioural risk factors.[10,26,36,37]

Rationale & Purpose

Data on the relationship between behavioural risk factors (e.g. tobacco use, physical activity, unhealthy diets) and the prevalence of individual chronic conditions (e.g. diabetes, hypertension) have been reported elsewhere using nationally representative data from the Jamaica Health and Lifestyle Survey (JHLS) 2000/2001[38,39] and the JHLS 2007/2008.[40–44] However, no investigation of the social determinants of specific patterns or combinations of diseases has been undertaken to date. The first paper of the dissertation identified three distinct multimorbidity patterns (labelled *Metabolic, Vascular-Inflammatory,* and *Respiratory*) in the Jamaican population, using latent class analysis (LCA), in addition to a *Relatively*

Healthy class characterized by little to no morbidity. This second paper builds on that research by examining the association between social determinants of health and multimorbidity class membership, via analyses guided by a latent class model and the World Health Organization (WHO) Commission on Social Determinants of Health (CSDH) framework (Figure 1).

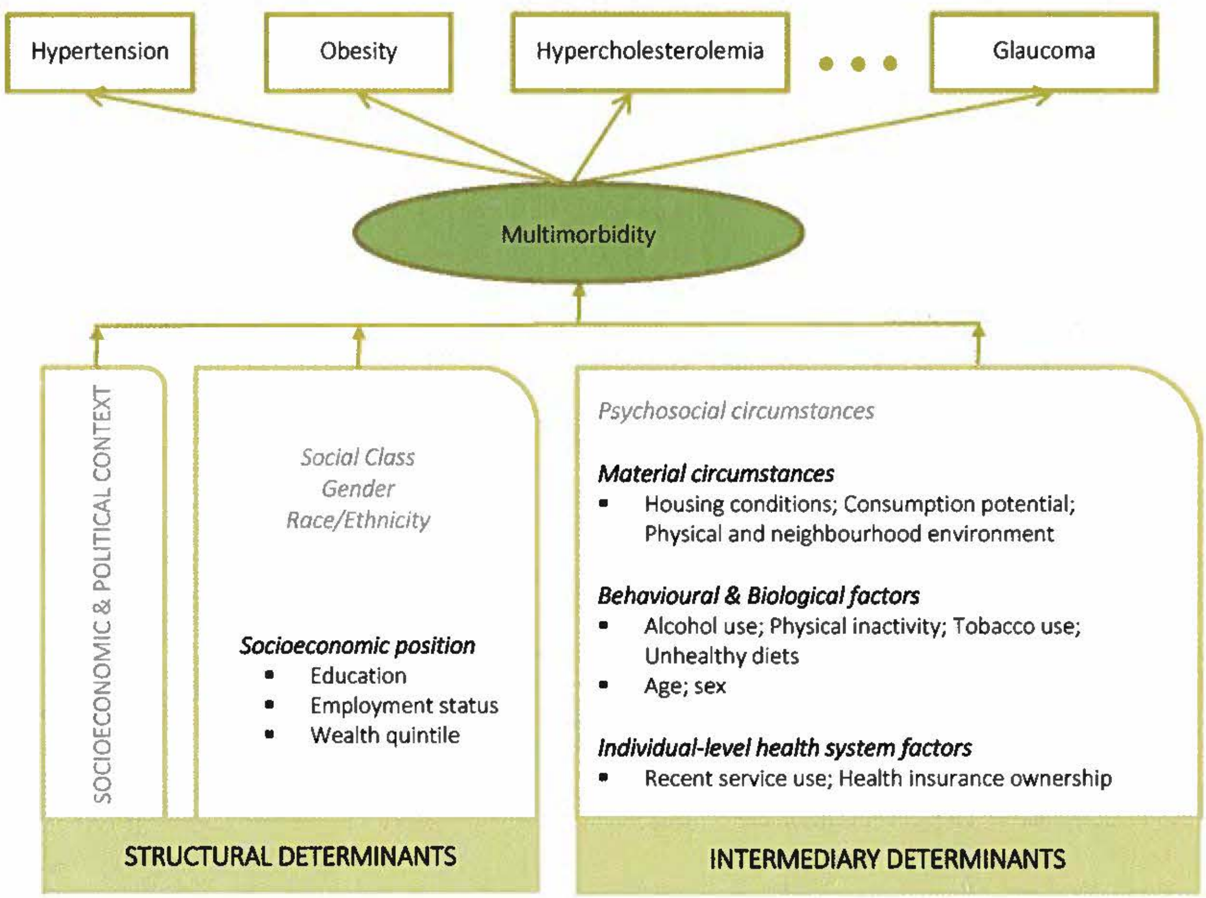

Figure 1. Conceptual framework for analysis of multimorbidity and its relationship with social determinants of health

Theoretical Framework

The CSDH model posits that our circumstances are shaped by the distribution of power, prestige and resources at global, national, and community levels, and that – aside from inherent genetic factors – the varying social, economic and political contexts into which we are born, live and work, engender differential exposure and differential vulnerability to the occurrence and intensity of ill-health and its consequences.[10] The framework emphasizes two main components (Figure 1).

1) **Structural determinants** reflect the joint role of the socioeconomic-polticial context and structural mechanisms in generating social stratification and assigning individuals to different social positions.[10] Specifically:
   - Socioeconomic-political context refers to the social, economic and political mechanisms that influence and maintain social hierarchies (e.g. governance, macroeconomic policies, social policies, public policies, cultural and societal values, and epidemiological conditions)[10]; and
   - Structural determinants and socio-economic position refer to aspects of the social structure which reinforce class divisions and define individual socio-economic position, according to the distribution of power, prestige and resources (e.g. income, education, occupation, social class, gender and race/ethnicity).[10]

2) **Intermediary determinants** reflect the individual level behaviours, biological processes and physiological factors which shape health outcomes.[10] Main categories of intermediary determinants include:
   - <u>Material circumstances:</u> housing conditions, neighbourhood quality, consumption potential, and physical and neighbourhood environments.[10]

- Psychosocial circumstances: psychosocial stressors (e.g. negative life events; job strain), stressful living circumstances (e.g. high debt), (lack of) social support and/or coping mechanisms.[10]
- Behavioural and biological factors: lifestyle factors such as tobacco smoking, unhealthy diets, alcohol consumption and lack of physical activity, in addition to genetic factors such as age and sex.[10]
- The health system: pertains to how health care access issues can influence differences in individual-level exposure and vulnerability, through health financing models as well as the early detection and treatment of disease[10]

Methods

Data

The JHLS-II recruited a sample of 2,848 Jamaicans, between 15-74 years old of age, over a four-month period spanning from November 2007 and March 2008.[40,41] The study employed a multi-stage cluster sampling design, with participant recruitment based on a random selection of clusters (enumeration districts) proportionate to the size of the population within the 14 parishes of Jamaica.[40] Within each cluster, a random starting point was chosen and every 10th household systematically identified, with a single individual from each household being invited to participate.[40] An interviewer-administered questionnaire was used to obtain data on demographic characteristics, medical history and health behaviours, including physical (i.e. height, body weight, hip circumference, waist circumference) and biological (i.e. blood pressure, blood glucose, total cholesterol) measurements that were made in accordance with standardized protocols.[40,41] Further details of the survey design, sampling procedures and data collection methods are provided in the technical report.[40]

Measures

Variables used in this study included indicators of multimorbidity class membership (i.e. individual NCDs) and factors representing structural and intermediary determinants of health that were examined as predictors of class membership.

Multimorbidity

Indicators of multimorbidity class membership are all fully described in Paper 1. Briefly, measurement of multimorbidity was limited to those NCDs with the greatest burden in the population (i.e. prevalence greater than or equal to 1% in each sex). Following guidance from a 2011 systematic review on multimorbidity measurement that related diseases be combined,[7] cardiovascular disease (i.e. heart disease, myocardial infarction, and circulation problems) and mental health disorders (i.e. depression, anxiety, psychosis, and other mental health problems) were grouped together to enhance data quality. Self-reported diagnosis of bronchitis/pneumonia was used as a proxy indicator of chronic obstructive pulmonary disease (COPD).

The final list of conditions included hypertension, obesity, hypercholesterolemia, diabetes, asthma, arthritis, cardiovascular disease, mental health disorders, COPD, stroke, and glaucoma. Presence or absence of disease was largely based on self-report, with the exception of four diseases (obesity; hypertension; diabetes; hypercholesterolemia) where physical assessments were available and used alone, or in combination with self-reports, to increase measurement validity and reliability. Specifically, objective measurements of height and weight were used to determine obesity status (BMI ≥ 30 kg/m^2), in accordance with WHO guidelines.[1] Diabetes was defined as having a fasting plasma glucose value ≥ 7.0 mmol/L (126 mg/dl) or being on medication for raised blood glucose.[1] Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or using medication to lower blood pressure.[1] Hypercholesterolemia was defined as total cholesterol levels of 5.2 mmol/l or higher or self-reported use of medications to control blood cholesterol.[1]

Social determinants of health

Structural Determinants

The CSDH framework identifies occupational status, educational attainment and income level as the most important structural stratification indicators, often used to operationalize socio-economic position.[10] In this study, binary indicators of occupational status and educational attainment were used to classify participants as being employed full-time (yes/no) and having attained at least secondary level education or equivalent (yes/no), respectively. It was hypothesized that full-time employment and higher educational attainment would be negatively associated with multimorbidity, based on evidence from the literature of greater risk of chronic NCDs (i.e. diabetes, hypertension, cardiovascular disease) among Jamaicans in lower socio-economic categories (based on occupation and education) compared to those in higher socio-economic categories.[42,44,45]

To determine income level, principal component analysis (PCA) was used to generate a wealth index, based on responses (i.e. yes/no) to several questions on household assets (i.e. ownership of gas/electric stove, refrigerator or freezer, microwave oven, telephone, radio, television set, cable, satellite dish, bicycle, motorbike, car, computer, washing machine, sewing machine, fan, air conditioner, compact disk (CD) player, stereo equipment, record player, and video cassette recorder) and living conditions (i.e. number of members per sleeping room). The wealth variable was categorized into quintiles (i.e. poorest to wealthiest) and then dichotomized to reflect those in the top 60% and bottom 40% wealth quintiles. Studies in Jamaica have identified significant relationships between wealth and chronic disease prevalence, particularly among women, with lower prevalence of diabetes observed among Jamaican women with higher income[42] but greater burden of hypertension among the wealthiest women compared to women in intermediate income groups.[46] Nonetheless, given evidence from low- and middle-income settings of a significant positive association between multimorbidity and increasing wealth, it was hypothesized that being in the top 40% wealth quintile would be positively associated with multimorbidity.

Neither measures of the socioeconomic-political context nor other social stratification indicators (e.g. social class, gender) could be operationalized from available data. Further, data on race/ethnicity were not included – though available – since the majority of the sample population (93.79%) identified as black.

Intermediary determinants

Material circumstances. The indicator for housing conditions was created by summing scores reflecting the interviewer's assessment of specific characteristics of the respondent's home (i.e. the physical condition of the home; internal cleanliness of the home, physical condition of the furnishings, external appearance of the home). Interviewers rated each characteristic from 1 (excellent) to 4 (poor). The Cronbach's alpha internal consistency coefficient of this home quality summated scale was 0.96 – exceeding the minimum acceptable value of 0.70.[47] Items were reversed scored so that higher summed scores were taken as indicative of more favourable home environments. Studies have suggested that greater home disorder is associated with lower odds of overweight/obesity among Jamaicans.[43] It was thus hypothesized that more favourable home environments would be positively associated with multimorbidity.

Guided by Kerr and colleagues (2012) theoretical model of the role of neighbourhood environments in supporting positive health outcomes, four specific aspects of the built and social environment were examined to reflect: (1) walkability (i.e. the ease of access to destinations); (2) access to parks and recreational amenities; (3) safety; and (4) aesthetics (including the availability of sidewalks and pleasant scenery).[48] It was hypothesized that these favourable aspects of the built environment would be negatively associated with multimorbidity. The binary variable for walkability reflected the interviewer's assessment of whether a place to obtain fresh fruits and vegetables was within walking distance of the participant's home. A similar variable was created for access to parks and recreational amenities to reflect the interviewer's assessment of whether recreation areas were within walking distance of the home. Perceived safety of the community was assessed using the question "How safe is it to walk in your community", with responses on a 5-item scale ranging from very safe (1) to very dangerous (5). Responses were collapsed to create a dichotomous indicator of greater (i.e. very safe or safe) and lesser (i.e. usually safe, can be dangerous, very dangerous) perceived safety. For aesthetics, an index was created to reflect the neighbourhood infrastructure. Specifically, interviewer responses regarding the presence (1) or absence (0) of specific features in the respondent's community (e.g. paved roads, sidewalks, electricity supply to homes, telephone lines to homes, street lighting, clean streets, and recreation areas/ playing field/open spaces) were summed. The Cronbach's alpha internal consistency coefficient of the neighbourhood infrastructure scale was 0.71, with higher overall scores indicative of more favourable circumstances.

Behavioural risk factors. Behavioural risk factors such as tobacco smoking, alcohol use, low physical activity levels and unhealthy dietary patterns are well-established risk factors for individual chronic diseases.[49] Accordingly, it was hypothesized that these unhealthy lifestyle behaviours would be positively associated with multimorbidity.

Dichotomous indicators of tobacco smoking and alcohol use were created to reflect past or current tobacco use (yes/no) and current alcohol drinkers (yes/no), respectively. Physical activity levels were determined based on responses to the International Physical Activity Questionnaire (IPAQ)- Short Form. In accordance with data cleaning guidelines for the IPAQ short form, the following rules were observed when creating walking, moderate-intensity activity and vigorous-intensity activity scores: (1) responses to physical activity duration (time) were converted from hours and minutes into minutes; (2) values of '15', '30', '45', '60' and '90' "hours" were converted to '15', '30', '45', '60' and '90' "minutes", respectively; (3) unreasonably high data (i.e. where the sum of all walking, moderate and vigorous time variables exceeded 960 minutes) were excluded from analysis; (4) only values of 10 or more minutes of activity were included in the calculation of summary scores and responses of less than 10 minutes (along with their associated days) were re-coded to '0'; and (5) all walking, moderate and vigorous time variables exceeding '180 minutes' were truncated to be equal to 180 minutes.[50] Metabolic equivalent (MET) levels were determined using scores on walking, moderate-intensity activity and vigorous-intensity activity, and used to create categories based on established cut-offs, reflecting high (i.e. ≥ 7 or more days of any combination of walking, moderate- or vigorous-intensity activities accumulating at least 3000 MET-minutes/week), moderate (i.e. ≥ 5 days of any combination of walking, moderate- or vigorous-intensity activities achieving a minimum of at least 600 MET-minutes/week) or low (i.e. no activity or some activity reported but not enough to meet moderate or high levels).[50] The moderate- and high-intensity categories were then collapsed and a binary indicator reflecting low (yes/no) levels physical activity created.

Unhealthy diets were examined using two measures: (1) high fast food consumption; and (2) sugar-sweetened beverage (SSB) intake. Levels of salt and sugar intake have been receiving increased attention in the NCD literature, with evidence suggesting that both higher dietary salt intake[49] and higher SSB consumption[51,52] are associated with increased risk of individual NCDs. Among Jamaican adolescents (i.e. 15-19 years old), studies have shown that increased fast food consumption (i.e. at least four times per week) and increased consumption of SSBs (i.e. more than one bottle daily) are independently associated with being overweight.[53] To assess high fast food consumption, a dichotomous variable was created to reflect those respondents who reported eating at fast food places such as Burger King, KFC, Tastee, Juici Patties or Pizza Hut at least twice per week. This definition has been used in previous studies assessing excessive fast food consumption.[54] In this study, SSBs were defined as soft drinks (i.e. sodas), fruit drinks (i.e. box drinks) and lemonade. Using data from the JHLS-II food frequency questionnaire, high SSB intake included those who reported drinking lemonade/soda/box drink at least daily. This definition has been used in previous studies.[51,52]

Biological factors included sex (i.e. male or female) and age, which was treated as a continuous variable and included all persons 15-74 years.

Health system factors. Individual-level health system factors were assessed using two dichotomous indicators of (1) private insurance ownership; and (2) recent health service use. To gauge access to health care services, a binary indicator was created to reflect whether or not the participant owned private insurance. Studies have shown that private insurance ownership is associated with better control of diabetes among Jamaicans, suggesting the importance of greater access to care in chronic disease prevention and control.[42] It was thus expected that, via improved access to care (to facilitate early risk detection and prompt treatment), private insurance ownership would be negatively associated with multimorbidity. Timing since the respondent last had his/her blood pressure measured was used as a proxy indicator of a recent health service visit. Respondents who reported that their last blood pressure measurement was less than 6 months ago were coded as having a recent health care visit. It was hypothesized that recent health care visits would be positively associated with multimorbidity since international studies have associated increased health care utilisation with prevalent multimorbidity.[55-57]

Statistical Approach

Analyses were restricted to participants with non-missing information on the 11 NCD multimorbidity indicators. Of the 2,848 respondents who completed the survey, 311 (10.9%) were missing information on one or more of these indicators. There were no statistically significant differences between those with complete and those with missing information on the basis on sex, age or region of residence. The final analytic sample of 2,551 respondents included 790 males and 1,761 females.

Descriptive statistics were calculated for each age and sex group, to determine the prevalence of morbidity (from individual NCDs) and multimorbidity. Means with 95% confidence intervals (for continuous variables), and proportions (for categorial variables) were computed and compared using the Mann-Whitney U test and the Pearson χ^2 statistic, respectively, to examine differences across age and sex groups. All analyses were weighted using sampling weights, to account for differences in sampling selection probabilities, in addition to post-stratification weights, to account for differences in the age-sex distribution of the study sample compared to the Jamaican population. In accordance with recommended research practice, however, regressions were unweighted.[58]

Latent Class Analysis (LCA)

LCA was used to determine NCD multimorbidity patterns based on the presence/absence of 11 NCDs. This involved fitting a series of models to the data, starting with a one-class model and increasing classes in a stepwise fashion until model fit no longer significantly improved. To determine the baseline model, several indices were compared, including the likelihood-ratio G^2 statistic, the Akaike Information Criteria (AIC), the Bayesian Information Criteria (BIC) and the adjusted BIC, with lower values suggestive of a more optimal fit.[59,60] Probability plots for the latent classes were also inspected to consider the substantive interpretability (i.e. the meaningfulness and distinctiveness) of the resultant latent class solutions.[59] Steps used to determine the baseline LCA model are described in greater detail in Paper 1.

Multinomial Logistic Regression models

Once the baseline model was identified, participants were assigned to their best fit class based on their maximum posterior probability of class membership. Each class was treated as a dependent variable and analyses performed using multinomial logistic regression. Multinomial logit models are used for nominal variables, which lack a natural ordering. These models simultaneously estimate the effects of the independent variables, for all but one outcome which is selected to reflect the baseline reference category. In this study, the *Relatively Healthy* was selected as the base category to which other multimorbidity patterns were compared. Regression coefficients were exponentiated to yield relative risk ratios (RRR) and 95% confidence intervals (95% CI), for a unit change in the predictor variable, reflecting the relative risk or the ratio of the probability of membership in one outcome category over the probability of membership in the baseline *Relatively Healthy* class.

As a first step towards building multivariate models, unadjusted multinomial regression analyses were conducted for each social determinant of health to examine the crude relationship of each indicator with the identified latent classes. This step allowed for description of the social composition of identified patterns as well as identification of significant predictors for inclusion in subsequent multivariate models. Any variable found to be a significant predictor of one or more multimorbidity patterns was included in the final model. The absence of multi-collinearity was also tested, using the variance inflation factor (VIF), to ensure robustness of the regression models. Then, guided by the WHO CSDH framework (Figure 1), a series of multivariate multinomial logistic regression models were run to control for the potentially confounding effects of other indicators. Authors of the CSDH model note that while intermediary determinants are closely tied to both socio-economic position and health outcomes, the association between socio-economic position and health is often reduced, though not eliminated, upon statistically controlling for these determinants. Accordingly, multivariate regression models were performed as a series of steps, where Model 1 included structural determinants (i.e. socio-economic position) only, Model 2 included intermediary determinants only, and Model 3 included all social determinants of health.

As a final step towards ensuring that the multinomial regression was well-specified, the independence of irrelevant alternatives (IIA) test was performed. Generally speaking, multinomial models assume that outcome categories of the model have the property of IIA, meaning that inclusion or exclusion of categories does not affect the relative risks associated with the regressors in the remaining categories.[61,62] Under the IIA assumption, no systematic change in the coefficients is expected upon excluding one of the outcomes (i.e. one of the multimorbidity classes) from the model.[61,62] To test the IIA assumption, a Hausman test was performed by first estimating the full multinomial model (i.e. Model 3) with all multimorbidity latent classes and then estimating a restricted model, with one of the outcomes excluded. Results of the Hausman test provided no evidence that the IIA assumption had been violated, indicating that the null hypothesis of no systematic difference in coefficients could not be rejected [Hausman statistic $\chi^2 = 1.53$, df = 32, $p = 0.999$]. In other words, there was no evidence against the correct specification of the multinomial model for multimorbidity patterns in the sample.

All statistical analyses were carried out using Stata v.15 software, with a value of $p< 0.05$ regarded as statistically significant.

RESULTS

Sample description

Descriptive statistics for the weighted sample, according to age-group, are presented in Table 1 (see also Table A1). There were significant differences across 10-year age-groupings for all NCDs, except mental health disorders and COPD. Generally speaking, NCD prevalence increased with advancing age, with the exception of asthma where slightly lower prevalence was observed across older age-groups.

Nearly, one-quarter (24.05%) of the sample population was multimorbid (i.e. had two or more diseases). Similar to the prevalence of individual NCDs, the burden of multimorbidity significantly increased with advancing age (15-24 years=7.44% vs. 25-34 years=10.50% vs. 35-44 years=24.16% vs. 45-54 years=42.13% vs. 55-64 years=51.12% vs. 65-74 years=64.01%; $p<0.001$). The mean number of NCDs reported also increased with successive age-groups ($p<0.001$). Using a more discriminating definition of multimorbidity (i.e. three or more diseases), significant differences across age-groups were also observed with a prevalence of 0.89% among those 15-24 years of age while over one third (35.56%) of those 65-74 years of age were affected ($p<0.001$).

LCA results

LCA results are described fully in Paper 1. To summarize, the final model comprised 4 classes: a *Relatively Healthy* class (52.70%) with little to no morbidity; a *Metabolic* class (30.88%) characterized by high likelihood of self-reporting hypertension and obesity; a *Vascular-Inflammatory* class (12.21%) characterized by individuals with a high probability of self-reporting hypertension, obesity, diabetes, hypercholesterolemia, arthritis and cardiovascular disease; and a *Respiratory* class (4.20%) characterized by increased likelihood of self-reporting asthma and COPD.

Table 1. Prevalence of Select Non-Communicable Diseases (NCDs) by age-group (JHLS-II data, 2007/2008; N=2,551)

	15-24 (n=464)	25-34 (n=519)	35-44 (n=531)	45-54 (n=475)	55-64 (n=296)	65-74 (n=266)	All ages (N=2,551)
NCD Prevalence							
Hypertension***	6.43	11.38	22.97	47.31	59.66	67.03	25.33
Obesity***	12.39	24.12	32.55	34.74	30.11	27.66	25.23
Hypercholesterolemia***	3.85	7.25	12.18	19.50	22.18	24.21	11.53
Diabetes mellitus***	1.12	2.32	6.89	14.28	18.02	30.37	7.86
Asthma*	9.79	6.23	6.66	6.38	3.48	3.64	6.85
Arthritis***	0.13	1.13	3.16	5.75	18.04	29.01	5.24
Cardiovascular disease***	1.73	1.66	3.53	6.67	11.03	17.42	4.62
Mental health disorders	2.95	3.01	3.31	2.84	3.52	1.25	2.96
COPD	2.52	2.94	2.08	4.79	2.66	2.04	2.80
Stroke***	0.18	0.41	0.47	2.08	3.27	6.16	1.21
Glaucoma***	0.00	0.11	0.99	0.75	3.08	7.33	1.10
Multimorbidity (2+ NCDs)***	7.44	10.50	24.16	42.13	51.12	64.01	24.05
Multimorbidity (3+ NCDs)***	0.89	4.13	8.06	19.67	25.29	35.56	10.16
Mean number of NCDs reported (95% CI)***	0.41 (0.34, 0.48)	0.61 (0.52, 0.70)	0.95 (0.85, 1.04)	1.45 (1.30, 1.60)	1.75 (1.58, 1.92)	2.16 (1.98, 2.34)	0.95 (0.90, 0.99)

COPD = chronic obstructive pulmonary disease

Note: Values are weighted proportions or mean (95% CI)

p-value for difference across age-groups based on chi-squared (χ^2) test or and Mann-Whitney U test, as appropriate (*p<0.05; **p<0.01; ***p<0.001)

Social composition of Multimorbidity Patterns

There were significant differences in the social patterning of multimorbidity according to structural determinants and socio-economic position (i.e. education level, employment status, wealth quintile) and intermediary determinants of health (i.e. proximity to destinations, home environment quality, current alcohol use, past or current smoking status, low physical activity levels, excessive fast food consumption, SSB intake, insurance ownership, recent health service use). Table 2 shows the social characteristics of each class, as well as the bivariate association of each determinant with the three multimorbidity patterns.

With regard to structural determinants and socio-economic position, and compared to those in the *Relatively Healthy* class, individuals in the *Metabolic* class were less educated and less wealthy while individuals in the *Vascular-Inflammatory* class were less educated and less likely to be employed full-time. Individuals in the *Respiratory* class were more likely to be employed full-time than their *Relatively Healthy* counterparts.

Regarding intermediary determinants, individuals in the *Metabolic* class were more likely to have better housing conditions, less likely to currently use alcohol, more likely to be a past or present smoker, and less likely to consume fast food excessively, than those in the *Relatively Healthy* class. Individuals in the *Vascular-Inflammatory* class were also more likely have better housing conditions than their *Relatively Healthy* counterparts, but less likely to live in close proximity (i.e. walking distance) to recreation areas or a place where fruits and vegetables could be obtained. These individuals were also less likely to use alcohol, more likely to report low levels of physical activity, and less likely to either partake in either excessive fast food consumption or daily consumption of SSBs. Compared to those in the *Relatively Healthy* class, individuals in the *Respiratory* class were more likely to report lower levels of physical activity.

Table 2. Respondent characteristics and bivariate association of social determinants of health with multimorbidity patterns (JHLS-II data, 2007/2008; N=2,551)

	Relatively Healthy (n=1,523)		Metabolic (n=717)		Vascular-Inflammatory (=254)		Respiratory (n=57)	
	%	RR	%	RR	%	RR	%	RR
Structural determinants								
Socio-economic position								
Secondary level or higher	77.73	1.00	50.40	0.28*** (0.23, 0.34)	39.01	0.18*** (0.13, 0.24)	77.72	0.85 (0.48, 1.52)
Employed full-time	44.33	1.00	48.48	0.96 (0.80, 1.15)	31.77	0.60*** (0.46, 0.80)	60.52	1.72* (1.01, 2.94)
Top 60% wealth quintile	66.61	1.00	62.89	0.81* (0.68, 0.97)	61.59	0.80 (0.61, 1.04)	74.74	1.32 (0.75, 2.33)
Intermediary determinants								
Material Circumstances								
Housing conditions (mean, 95% CI)	10.60 (10.20, 11.00)	1.00	11.06 (10.60, 11.50)	1.05** (1.02, 1.08)	11.42 (10.93, 11.91)	1.09*** (1.04, 1.14)	10.86 (9.73, 11.99)	1.04 (0.96, 1.14)
Place to obtain fruit & vegetables (in walking distance)	55.19	1.00	54.33	0.89 (0.74, 1.07)	46.43	0.63** (0.48, 0.84)	52.41	0.79 (0.46, 1.36)
Recreational areas in walking distance	49.15	1.00	49.24	0.91 (0.75, 1.10)	41.89	0.69* (0.52, 0.92)	55.85	1.06 (0.62, 1.82)
Greater perceived safety	64.64	1.00	72.96	1.17 (0.97, 1.42)	69.65	1.31 (0.97, 1.77)	72.35	1.39 (0.76, 2.52)
Neighbourhood infrastructure score (mean, 95% CI)	5.22 (5.00, 5.44)	1.00	5.16 (4.93, 5.40)	0.98 (0.93, 1.04)	5.16 (4.89, 5.44)	0.96 (0.88, 1.04)	5.26 (4.90, 5.63)	0.99 (0.84, 1.17)
Behavioural risk factors								
Currently use alcohol	69.41	1.00	57.53	0.57*** (0.48, 0.68)	44.14	0.42*** (0.32, 0.55)	69.94	1.04 (0.60, 1.80)
Past of present smoker	30.62	1.00	34.71	1.22* (1.01, 1.48)	32.43	1.11 (0.82, 1.48)	24.84	0.83 (0.44, 1.56)
Low levels of physical activity	52.15	1.00	52.46	1.09 (0.91, 1.30)	64.29	1.69*** (1.28, 2.24)	75.38	2.04* (1.15, 3.63)
Excessive fast food consumption	13.94	1.00	6.40	0.33*** (0.22, 0.48)	4.33	0.21*** (0.10, 0.44)	5.60	0.40 (0.12, 1.29)

Consumes SSB at least once daily	50.27	1.00	49.31	0.93 (0.78, 1.12)	39.45	0.70** (0.53, 0.91)	57.35	0.90 (0.53, 1.54)
Biological risk factors								
Age (mean, 95% CI)	31.98 (31.57, 32.40)	1.00	46.07 (45.03, 47.11)	1.08*** (1.07, 1.08)	56.51 (54.66, 58.36)	1.13*** (1.11, 1.14)	37.90 (33.40, 42.39)	1.04*** (1.02, 1.06)
Female sex	49.53	1.00	48.71	1.08 (0.90, 1.31)	74.86	2.48*** (1.76, 3.50)	69.92	3.09** (1.45, 6.58)
Health System Factors								
Insurance ownership	18.82	1.00	16.13	0.76* (0.59, 0.98)	27.05	1.61** (1.18, 2.20)**	25.76	1.16 (0.59, 2.28)
Recent health service use	39.08	1.00	54.95	2.01*** (1.67, 2.41)	82.57	6.75*** (4.73, 9.64)	79.56	4.05*** (2.16, 7.60)

CI = confidence interval; RR = risk ratio
<10% missing data
(*p<0.05; **p<0.01; ***p<0.001)

Individuals across all multimorbidity classes were generally older than their *Relatively Healthy* counterparts, while those in the *Vascular-Inflammatory* and *Respiratory* classes were more likely to be female. Finally, with regard to health system factors, the *Metabolic* class was less likely, and the *Vascular-Inflammatory* class more likely, to report private insurance ownership, compared to the *Relatively Healthy* class. Recent health service use was consistently reported across all multimorbidity patterns.

Multinomial Logistic Regression Analyses

The VIF for each variable was below the cut-off value of 10,[63] suggesting that multicollinearity was not a problem in subsequent multivariate models. Results of the multivariate, multinomial regression models are presented in Table 3.

In the model with structural determinants only (Model 1), higher educational attainment was associated with lower likelihood of membership in either the *Metabolic* (RRR = 0.27; 95% CI: 0.22, 0.33) or *Vascular-Inflammatory* (RRR = 0.17; 95% CI: 0.12, 0.22) class. Further, a significant inverse relationship was observed between fulltime employment (RRR = 0.61, 95% CI: 0.46, 0.82) and membership in the *Vascular-Inflammatory* class, while a significant positive relationship was observed between membership in this class and being among the top 60% wealth quintile (RRR = 1.38; 95% CI: 1.03, 1.85).

In the model with only intermediary determinants (Model 2), significant associations were observed with biological risk factors and health system factors, only. Advancing age was a significant predictor of all three multimorbidity patterns ($RRR_{Metabolic}$= 1.07, 95% CI: 1.06, 1.08; $RRR_{Vascular\text{-}Inflammatory}$= 1.12, 95% CI: 1.11, 1.14; $RRR_{Respiratory}$= 1.04, 95% CI: 1.02, 1.07). Being female increased the likelihood of membership in the *Vascular-Inflammatory* (RRR = 2.65, 95% CI: 1.64, 4.28) class. Private insurance ownership (RRR = 0.60, 95% CI: 0.44, 0.83) was associated with lower likelihood of belonging to the *Metabolic* class.

Table 3. Multivariate multinomial logistic regression results of multimorbidity patterns and social determinants of health (JHLS-II data, 2007/2008; N=2,551)

	Model 1 – Structural determinants only			Model 2 – Intermediary determinants only			Model 3 - All Social Determinants of Health		
	Metabolic	Vascular-Inflammatory	Respiratory	Metabolic	Vascular-Inflammatory	Respiratory	Metabolic	Vascular-Inflammatory	Respiratory
Structural determinants									
Socio-economic position									
Secondary level or higher	0.27*** (0.22,0.33)	0.17*** (0.12,0.22)	0.77 (0.42,1.41)				0.73* (0.56,0.96)	0.87 (0.57,1.35)	1.03 (0.50,2.16)
Employed full-time	0.97 (0.80,1.17)	0.61*** (0.46,0.82)	1.69 (0.99,2.89)				0.90 (0.72,1.13)	0.76 (0.52,1.09)	1.68 (0.92,3.07)
Top 60% wealth quintile	1.16 (0.95,1.42)	1.38* (1.03,1.85)	1.34 (0.74,2.42)				1.18 (0.91,1.53)	1.33 (0.89,1.98)	1.56 (0.77,3.19)
Intermediary determinants									
Material Circumstances									
Place to obtain fruit & vegetables (in walking distance)				1.06 (0.83,1.36)	0.86 (0.58,1.27)	0.96 (0.49,1.86)	1.04 (0.81,1.34)	0.84 (0.56,1.25)	0.93 (0.48,1.81)
Recreational areas in walking distance				0.90 (0.70,1.16)	0.72 (0.48,1.07)	0.85 (0.43,1.66)	0.94 (0.73,1.21)	0.71 (0.47,1.07)	0.79 (0.40,1.56)
Home quality (mean, 95% CI)				1.03 (0.99,1.07)	1.03 (0.97,1.09)	1.01 (0.91,1.11)	1.03 (0.99,1.07)	1.01 (0.95,1.08)	0.98 (0.89,1.09)
Behavioural risk factors									
Currently use alcohol				0.81 (0.63,1.02)	0.95 (0.66,1.38)	1.51 (0.81,2.81)	0.79 (0.62,1.01)	0.91 (0.63,1.33)	1.42 (0.76,2.66)
Past of present smoker				1.09 (0.83,1.41)	1.27 (0.84,1.92)	0.54 (0.24,1.22)	1.10 (0.84,1.43)	1.27 (0.84,1.92)	0.58 (0.25,1.33)
Low levels of physical activity				1.05 (0.84,1.31)	1.24 (0.87,1.77)	1.73 (0.92,3.26)	1.04 (0.83,1.30)	1.21 (0.84,1.73)	1.83 (0.97,3.45)
Excessive fast food consumption				0.85 (0.54,1.36)	0.98 (0.39,2.43)	0.73 (0.21,2.51)	0.85 (0.54,1.35)	0.94 (0.38,2.36)	0.71 (0.21,2.45)
Consumes SSB at least once daily				1.07 (0.86,1.34)	0.91 (0.65,1.29)	1.03 (0.58,1.85)	1.07 (0.86,1.33)	0.89 (0.63,1.26)	1.05 (0.58,1.89)

Biological risk factors						
Age (mean, 95% CI)	1.07*** (1.06,1.08)	1.12*** (1.11,1.14)	1.04*** (1.02,1.07)	1.06*** (1.05,1.08)	1.12*** (1.10,1.14)	1.05*** (1.02,1.07)
Female sex	1.04 (0.79,1.36)	2.65*** (1.64,4.28)	1.77 (0.76,4.13)	1.02 (0.78,1.35)	2.54*** (1.56,4.11)	1.95 (0.83,4.60)
Health System Factors						
Insurance ownership	0.60** (0.44,0.83)	1.33 (0.87,2.03)	0.90 (0.42,1.92)	0.63** (0.45,0.87)	1.32 (0.85,2.06)	0.76 (0.35,1.66)
Recent health service use	1.71*** (1.36,2.16)	3.64*** (2.38,5.56)	3.77*** (1.82,7.81)	1.68*** (1.33,2.12)	3.60*** (2.35,5.51)	3.57*** (1.72,7.41)

<10% missing data
(*p<0.05; **p<0.01; ***p<0.001)

All multimorbidity classes were significantly associated with recent health service use ($RRR_{Metabolic}$= 1.71, 95% CI: 1.36, 2.16; $RRR_{Vascular-Inflammatory}$= 3.64, 95% CI: 2.38, 5.56; $RRR_{Respiratory}$= 3.77, 95% CI: 1.82, 7.81).

After adjusting for all social determinants of health (Model 3), advancing age (p<0.001) and recent service use (p<0.001) remained significant independent predictors of all multimorbidity classes. Female sex remained a significant independent predictor of membership in the *Vascular-Inflammatory* class (RRR = 2.54; 95% CI: 1.56, 4.11) while higher educational attainment (RRR = 0.73; 95% CI: 0.56, 0.96) and private insurance ownership (RRR = 0.63; 95% CI: 0.45, 0.87) maintained a significant inverse association with membership in the *Metabolic* class . After controlling for all determinants in Model 3, neither educational attainment, employment status nor wealth remained significant predictors of membership in the *Vascular-Inflammatory* class.

Discussion

This is the first study to examine the social patterning of multimorbidity in Jamaica. Building on the latent classes identified in Paper 1, this study shows that beyond differences in the type and number of diseases comprising multimorbidity patterns, there are also important social differences associated with class membership. Specifically, the study found that advancing age and recent health service use were significantly associated with all multimorbidity patterns. Female sex, lower educational attainment and lack of insurance were also independently associated with prevalent multimorbidity – although the significance varied across patterns.

Most international studies on the social patterning of multimorbidity have focused on structural determinants (i.e. mainly, socio-economic position) and biological factors. These studies often used simple counts of diseases, with fewer investigations exploring the relationships across patterns or with more intermediary determinants of health. Nonetheless, evidence from these studies suggests a social gradient to multimorbidity, with higher burden among the socio-economically disadvantaged (i.e. less educated, unemployed, lower wealth quintiles).[28,32,56] In this study, lower educational attainment in both *Metabolic* and *Vascular-Inflammatory* classes (compared to the *Relatively Healthy* class) is consistent with the literature on multimorbidity.[31,32,34,55,56,64] However, this difference only remained statistically significant among individuals exhibiting the *Metabolic* multimorbidity pattern, after controlling for all social determinants of health.

Among biological factors, age has been well-established as a strong risk factor for chronic disease multimorbidity.[5,7,28] Similarly, in this study, advancing age was a significant independent predictor of all 3 multimorbidity patterns. Notably, however, while the mean age of individuals in the *Metabolic* and *Vascular-Inflammatory* classes was 46.07 years (95% CI: 45.03, 47.11) and 56.51 years (95% CI: 54.66, 58.36), respectively, the age-profile of the *Respiratory* class (mean age: 37.90 years; 95% CI: 33.40, 42.39) suggested that this pattern comprised relatively young adults. This finding reflects the fact that multimorbidity is not solely a problem of old age and reinforces the need for prevention efforts across the life course to curb the accumulation of NCDs and promote healthy ageing. Evidence from the 2011 Jamaican population census confirmed a shift in the age structure, with a decline in the under-15 year old population, an increase in the population over 60 years of age and the largest increase among the old-old (i.e. those 80 years and older).[65] Investigation of the burden and socio-economic patterning of multimorbidity among elderly populations in Jamaica would represent a useful next step, to further inform healthcare and social services planning and support improved health and quality of life in old age. Notably, LCA of multimorbidity profiles among German centenarians identified a "low morbidity" class (comprising 36% of the sample) with lower odds of hospitalization and long-term care facility use, highlighting the potential for minimal disease burden and good quality of life even at such an advanced age.[66]

Consistent with evidence of differences in multimorbidity patterns across sex, this study found that being female was associated with an increased risk of membership in the *Vascular-Inflammatory* class. Other studies in Jamaica[67,68], and the wider Caribbean region[69], have identified a female preponderance in morbidity from individual NCDs and it is not surprising then that women bear a greater burden of multimorbidity as well. Although this is likely due to a range of factors (such as better health-seeking behaviours facilitating disease diagnosis), causes of the gender disparity remain unclear and require further investigation. Notably, despite greater disease burden, life expectancy among Jamaican women is longer than that of men[70,71], suggesting that more in-depth exploration of lifestyle behaviours, social networks, and coping mechanisms among women may shed light on useful strategies to support management of multiple conditions.

With regard to intermediary determinants, material circumstances (i.e. features of neighbourhood environments) did not appear to be significant predictors of multimorbidity. This is somewhat in keeping with an earlier study in Jamaica which found no significant association between some environmental features – namely, perceptions of safety and availability of recreational spaces within walking distance – and individual NCDs (i.e. overweight/obesity and diabetes).[43] The relationship between insurance ownership and multimorbidity patterns is particularly interesting, with insurance ownership reducing the likelihood of membership in the *Metabolic* class relative to the *Relatively Healthy* class. Ability to purchase private health insurance may reflect increased financial capacity of these individuals and is in keeping with evidence from the literature that the accumulation of multiple morbidities is more common in the socio-economically deprived.[28,31] On the other hand, private insurance ownership may reflect better access to health care and lower likelihood of forging health care contact due to financial concerns, thereby facilitating the early recognition, prompt diagnosis and effective management of disease. Studies indicate that insurance ownership is indeed a significant predictor of health care utilization among older men in Jamaica.[70] Improved financial capacity and health care access through insurance ownership likely extends beyond disease detection to medication procurement and follow-up visits to physicians, suggesting the potential role of this enabling factor in multimorbidity control as well.

Increased health care utilization in association with multimorbidity has been consistently documented across studies, with a greater number of medical visits and more frequent hospitalizations among Spanish adults 50 years and older[56], higher odds of hospitalization and emergency department visits among American Medicare beneficiaries[55], and a preference for secondary outpatient care versus primary care among residents in southern China[31]. Consistent with available literature, results from this study indicated significant positive associations across all multimorbidity patterns with recent service use, although it is not clear whether this recent health service contact allowed for the diagnosis of conditions or was prompted in response to the burden of managing multiple conditions. Regardless, this finding alludes to the economic burden of multimorbidity faced by individuals and healthcare systems. A recent population-based Canadian study concluded that the relatively small proportion of the population with multimorbidity was responsible for a disproportionately large proportion of total healthcare costs, noting that the observed non-linearity in costs was likely attributed to complexity regarding the degree of multimorbidity and types of disease combinations.[72] Additional research using prospective follow-up to examine how multimorbidity patterns are associated with health service use, including primary care services, emergency department visits and hospital admissions, could better inform on health-seeking behaviours and the risk of adverse events, as well as the costs borne to individuals in managing prevalent diseases and preventing the accumulation of new ones. Importantly, health service use in Caribbean settings is often not limited to bio-medical therapies,[73,74] with previous studies indicating that among Jamaican adults, use of herbal remedies (concomitantly with pharmaceutical treatments) is common, particularly for respiratory system ailments and, among the uninsured.[75] Appreciation of the role of alternative medicines in the management of multimorbidity may have important health system implications regarding medication compliance, adherence to physician recommendations and risk of adverse drug events, to inform physician-patient interactions and public policy.

Strengths & Limitations

Although use of the nationally, representative JHLS-II survey data is among the strengths of this analysis, there are several study limitations to be acknowledged. First of all, the cross-sectional study design limits causal interpretation and reverse causality remains a plausible explanation for associations identified. As a limitation of cross-sectional analyses, reverse causation reflects the inability to identify whether disease affected behaviour or behaviour affected disease. One example where the direction of association is unclear includes the relationship between health service use and multimorbidity, as it is plausible that more recent health service use is a marker of better health-seeking behaviour which would facilitate diagnosis of additional diseases and greater awareness of multiple conditions.

Secondly, since social determinants examined in this study were subject to data availability, there are limitations regarding both the definition and measurement of certain indicators as well as residual confounding due to variables not included in analyses. On the one hand, features of the neighbourhood environment were not based on formal or validated scales. Convenience measures used in this study could have potentially influenced the lack of significant associations observed while proximity indicators may not have been the most useful measures since (walking) distance may not be the sole determinant of use of particular services and amenities. It should be noted that measures of respondent's home and community environments, as well as assessment of whether the respondent lived in walking distance to services and amenities of interest, was based on the subjective interpretation of the person conducting the interview. This creates some concern regarding variability in assessment across different interviewers; however, among the strengths of the JHLS-II survey, the technical report notes that in addition to training and certification of interviewers prior to field work, duplicate measures were made by supervisors to ensure data quality, with evidence that good inter- and intra-observer reliabilities were maintained throughout the survey.[40] Yet, with regards to limitations of interviewer-based assessments, it is noted that perceptions of quality and proximity may not be same for the respondent and interviewer, such that the an interviewer-based evaluation may not accurately reflect individual-level perceptions, motivations and circumstances. However, good Cronbach's alpha coefficients support the internal consistency of the summative scales used while their use in a previous local study[43], allows for comparability and builds on previous research.

With regard to residual confounding, high non-response rates for some questionnaire items (e.g. household income) precluded their inclusion in analyses. Although a proxy indicator of wealth was created based on a weighted composite of measures (i.e. non-productive assets and living conditions), limitations of such an index are noted, including failure to capture asset quality, short-term interruptions and household shocks.[76] Finally, potentially informative social determinants of health, such as psychosocial factors (e.g. social interaction, social support) and material circumstances (e.g. number of children living with respondent) were omitted from the analysis since questionnaire items did not allow for operationalization of these concepts. The role of family structure in multimorbidity prevalence and control remains relatively understudied. Some scientists have speculated that child-care and child-rearing responsibilities may reduce self-care capacity through scheduling demands and uptake of socio-economic resources.[77] Alternatively, studies among Canadian[78] and Australian[79] adults have found multimorbidity to be positively associated with not living with children, suggesting that family and/or social support networks may play a role in health outcomes, including disease prevention and management. A recent study among older Jamaican men identified regular attendance at club/society/religious meetings and financial support from a son or daughter as significant predictors of prostate checks and routine doctors' visits, respectively.[70] Social support systems may thus play an important role in preventive service uptake, and further exploration is needed to determine whether these networks can be leveraged to support the effective management of disease and timely detection of complications that would halt the accumulation of multiple conditions.

Lastly, as with other latent variable models, misclassification error is reasonable with LCA, particularly with assignment of individuals to a best fit class using posterior probabilities, which does not account for classification uncertainty.[80,81] This limitation should be borne in mind in interpretation of the results. In addition, due to unequal class sizes and the smaller sub-sample of male (compared to female) respondents, the study was not powered to analyse the social patterning of multimorbidity separately, according to sex.

Conclusions

This study highlights differences in the social composition of multimorbidity classes, allowing for a more nuanced understanding of the socio-demographic profiles of multimorbidity patterns than would have been possible with simple counts of diseases. Overall, individuals with multimorbidity were older, female, less educated, and uninsured, with greater healthcare use. Future work should explore the social patterning of multimorbidity via longitudinal designs to better identify social factors implicated in the accumulation of multiple conditions and understand how individuals modify their behaviours to manage their multimorbidity. Furthermore, exploration of the relationship of various multimorbidity patterns with health care spending, emergency department visits and hospital admissions can provide targeted information for program planning, resource allocation, improved disease management and reduced complications. Given the potential of multimorbidity to erode financial security and compromise self-care capacity through the burden and complexity of managing multiple diseases, the impact of multimorbidity patterns on quality of life outcomes should also be investigated.

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Appendix

Table A1. Prevalence of Select Non-Communicable Diseases (NCDs) by age-group and sex (JHLS-II data, 2007/2008; N=2,551)

	Males							Females						
	15-24 (n=160)	25-34 (n=146)	35-44 (n=156)	45-54 (n=132)	55-64 (n=101)	65-74 (n=95)	All ages N=790)	15-24 (n=304)	25-34 (n=373)	35-44 (n=375)	44-54 (n=343)	55-64 (n=195)	65-74 (n=171)	All ages (n=1,761)
NCD Prevalence														
Hypertension	9.63	11.16	24.11	43.50	57.37	61.41	25.48***	3.24	11.56	21.90	51.17	61.97	72.17	25.18***
Obesity	8.14	9.04	12.53	22.61	12.93	11.27	11.97*	16.63	36.95	51.56	47.05	47.52	42.69	37.80***
Hypercholesterolemia	1.07	6.55	8.43	11.71	12.89	17.28	7.53**	6.62	7.85	15.75	27.40	31.59	30.57	15.33***
Diabetes mellitus	1.60	1.08	4.19	13.88	12.05	28.32	6.46***	0.63	3.37	9.46	14.69	24.07	32.24	9.19***
Asthma	7.93	3.57	6.56	5.93	3.40	3.12	5.67	11.64	8.49	6.75	6.83	3.56	4.12	7.97*
Arthritis	0.00	0.00	1.67	0.00	6.49	17.45	2.10***	0.26	2.08	4.57	11.59	29.74	39.62	8.22***
Cardiovascular disease	1.11	0.00	1.03	4.30	6.88	10.47	2.40***	2.36	3.07	5.91	9.07	15.23	23.80	6.72***
Mental health disorders	3.95	2.92	1.69	2.59	1.80	0.86	2.63	1.96	3.09	4.84	3.10	5.25	1.60	3.28
COPD	2.06	2.54	1.25	3.17	0.78	2.89	2.08	2.98	3.29	2.87	6.43	4.55	1.25	3.49
Stroke	0.00	0.00	0.61	3.07	1.25	8.28	1.23***	0.36	0.75	0.33	1.07	5.32	4.21	1.20***
Glaucoma	0.00	0.00	1.46	0.37	3.16	6.36	1.08***	0.00	0.20	0.54	1.13	3.00	8.23	1.13***
Multimorbidity (2+ NCDs)	5.61	4.16	13.15	30.49	36.31	51.06	16.11***	9.26	15.88	34.61	53.93	66.13	75.88	31.58***
Multimorbidity (3+ NCDs)	0.61	2.54	3.70	13.11	8.17	18.89	5.34***	1.18	5.49	12.20	26.33	42.63	50.84	14.73***
Mean number of NCDs reported (95% CI)	0.35 (0.24, 0.47)	0.37 (0.23, 0.51)	0.64 (0.50, 0.77)	1.11 (0.87, 1.35)	1.19 (0.97, 1.41)	1.68 (1.34, 2.02)	0.69 (0.63, 0.74)***	0.47 (0.38, 0.55)	0.81 (0.70, 0.91)	1.24 (1.12, 1.37)	1.80 (1.62, 1.98)	2.32 (2.08, 2.55)	2.60 (2.37, 2.84)	1.19 (1.14, 1.25)***

*p<0.05; **p<0.01; ***p<0.001 (Difference across age-groups)

THE IMPACT OF MULTIMORBIDITY PATTERNS ON HEALTH-RELATED QUALITY OF LIFE AMONG JAMAICANS

ABSTRACT (300 words)

Background: Multimorbidity and health-related quality of life (HRQoL) are bitterly intertwined. Multiple chronic conditions may act additively or synergistically to adversely affect physical and mental health functioning, while poorer HRQoL may contribute to the worsening of the course of diseases. Understanding the mechanisms through which specific combinations of diseases affect HRQoL outcomes can facilitate identification of factors which are amenable to intervention and guide efforts to support improved management and prevention of diseases.

Objectives: To examine whether multimorbidity classes differentially impact physical and mental health dimensions of HRQoL, and quantify indirect effects on the multimorbidity-HRQoL relationship that are mediated by health system factors pertaining to financial healthcare access and service use.

Design and Methods: Latent class analysis (LCA) was used to estimate associations between multimorbidity classes and HRQoL outcomes, using data from the nationally representative Jamaica Health and Lifestyle Survey 2007/2008. HRQoL was measured using the SF-12 health survey. Mediation analyses guided by the counterfactual approach explored indirect effects of insurance coverage and service use on the multimorbidity-HRQoL relationship.

Results: Class membership differentially predicted HRQoL outcomes. Compared to individuals in the *Relatively Healthy* class, *Vascular-Inflammatory* class membership was associated with lower physical functioning (β=-5.48; p<0.001) while membership in both *Vascular-Inflammatory* (β=-1.69; p<0.05) and *Respiratory* (β=-2.53; p<0.05) classes was associated with lower mental functioning. Small indirect effects were also observed, with 13.25% and 10.04% of the total effect of *Vascular-Inflammatory* and *Respiratory* class membership, respectively, on mental aspects of HRQoL mediated by service use.

Conclusions: Specific combinations of diseases differentially impacted HRQoL, demonstrating the clinical utility and predictive validity of multimorbidity latent classes. To better tailor interventions to support management of multiple conditions, additional research is needed to further elaborate personal experiences with healthcare and examine how health system factors reinforce or mitigate positive health-seeking behaviours, including timely use of services.

Introduction

Chronicity associated with non-communicable diseases (NCDs) imposes substantial health, economic and social burdens to affected individuals, whilst also creating concerns regarding the organization, availability and use of health systems to support timely and effective care. Individually, NCDs are responsible for substantial death and disability[1,2]; importantly, when two or more NCDs occur together (i.e. multimorbidity), health outcomes are further modified, as a result of increased burden of diseases and reduced coping strategies.[3,4] Indeed, studies have linked prevalent multimorbidity with heightened risk for poor health outcomes, including physical declines, more frequent use of health services, and reduced quality of life.[5] Among these outcome measures, health-related quality of life (HRQoL) – a multidimensional construct encompassing functioning and well-being in physical, emotional and social dimensions of life[6,7] – is of special importance in the multimorbidity literature. Given the lifelong experience of NCDs, as well as the potential for poorer physical and mental functioning to erode individual self-management capacity, intensify care demands, and contribute to a worsening of the course of diseases, HRQoL outcomes have important implications for management of existing conditions and prevention of additional morbidities.[3,6,8]

Several studies have explored the relationship between multimorbidity and HRQoL. A 2004 systematic review exploring the relationship between multimorbidity and quality of life outcomes among patients in primary care settings, confirmed a significant, inverse relationship between the number of medical conditions and HRQoL, related to physical domains.[6] Specifically, across the 30 studies included in this review, multimorbidity consistently predicted poorer physical functioning.[6] The relationship with mental dimensions of HRQoL was more varied, however, with most studies finding no statistically significant relationship while a few indicated significant declines in patients with 3, 4 or more concurrent diganoses.[6] The effect of multimorbidity on mental domains thus remains unclear, with commonly cited limitations of available evidence including the frequent exclusion of psychiatric diagnoses from multimorbidity measurement and the reliance on simple counts of diseases.[6] Researchers have suggested that multiple chronic conditions may act additively or synergistically to adversely affect health outcomes,[6,9,10] rendering the use of simple, crude counts ill-suited for examination of differential health effects associated with specific combinations of diseases.

Importantly, despite general consensus on the adverse effects of multimorbidity on the physical dimension of HRQoL, there is less agreement regarding the mechanistic pathways underlying poor HRQoL outcomes and the factors that may be amenable to intervention.[11] One possible pathway involves health system factors and may present opportunities for intervention. Some studies suggest that the role of the multimorbidity burden in predicting physical and mental health functioning outcomes is affected by the structure of health system, including instruments to support financial access to care and "hassles" associated with health system interaction (e.g. seeking information, scheduling visits, interacting with health care providers, accessing health care).[11,12] Further, specific combinations of diseases are posited to have differential effects on patient's experiences with accessing, using and enacting care, with potential to differentially affect outcomes.[8,11] A systematic review of qualitative data exploring patient's subjective experiences of multimorbidity identified financial burdens and frequent healthcare use among the most pressing components of individual experiences in managing the burden and treatment of multimorbidity.[12] Specifically, with regard to the financial burden, individuals reported that financial pressures were exacerbated by need for private insurance, as this often shaped user charges and the amount to be reimbursed.[12] On the other hand, frequent service use was noted to negatively impact individual's subjective experience of multimorbidity, by serving as a reminder to patients of all health problems which they currently faced.[12]

Rationale & Purpose

Health service delivery in Jamaica is organized via a two-tiered system with the public sector primarily responsible for a broad network of primary, secondary and tertiary care facilities (94% of the country's bed capacity) while the private sector mainly provides ambulatory services (75% of all outpatient care) and pharmaceuticals (82% of all sales).[13,14] The removal of user fees in public health facilities in 2008 enabled free access to care and was met with increased access to and use of health services from 2008-2009.[13] Unfortunately, this increased demand has also threatened service quality, with reports of long wait times, insufficient supplies, and inadequate human resources, noted to have driven Jamaicans from all income groups – including the poorest income quintiles – to increasingly seek private medical care.[13] To better support the population in managing NCDs, and in recognition of the fact that medication costs account for a substantial portion of out-of-pocket spending, the Government of Jamaica complemented its effort to improve financial access to care (i.e. via the abolition of user fees) with two government programs to enhance financial access to drugs: the Jamaica Drug for the Elderly (JADEP) program and the National Health Fund (NHF).[13] The JADEP provides subsidies for specific drugs covering 10 chronic illnesses for all residents of Jamaica over the age of 60 while the NHF provides subsidies to its beneficiaries for the treatment of 16 chronic diseases and is without age restrictions.[15] Unlike the JADEP program, however, enrolment in the NHF is need-based with potential beneficiaries needing to show proof of diagnosis of an eligible condition.

A systematic review of ten randomized controlled trials of interventions to improve outcomes for patients with multimorbidity, indicated that strategies targeting quality of life outcomes and functional difficulties were most promising, with evidence of a statistically significant reduction in mortality two years post-intervention.[16] Thus, improved understanding of the mechanisms through which health system factors, pertaining to financial access and use of services, influence quality of life outcomes can better guide the allocation of resources and organization of care, with important implications for multimorbidity prevention and control. The third and final paper of this dissertation research used latent class analysis (LCA) to assess the distribution of HRQoL scores conditional on class membership, in an effort to demonstrate the predictive validity and clinical utility of multimorbidity latent classes.[9,17] Multivariate regression analyses explored associations between multimorbidity patterns and HRQoL outcomes, relating to physical and mental health dimensions. Finally, the potential mediating effect of health system factors was measured, via examination of whether indicators of financial access and health service use operate along the pathway between multimorbidity class membership and HRQoL outcomes.

Theoretical framework

Via the conceptual framework described below (Figure 1), the contribution of health system factors to the multimorbidity-HRQoL relationship will be examined, with an aim to answer the following research questions:

1. Do specific combinations of diseases (i.e. multimorbidity patterns) differentially affect HRQoL, relating to physical and mental domains?
2. Do health system factors (i.e. insurance coverage; recent service use) mediate the relationship between multimorbidity and HRQoL?
3. Do health system factors (i.e. insurance coverage; recent service use) moderate the relationship between multimorbidity and HRQoL?

(1)

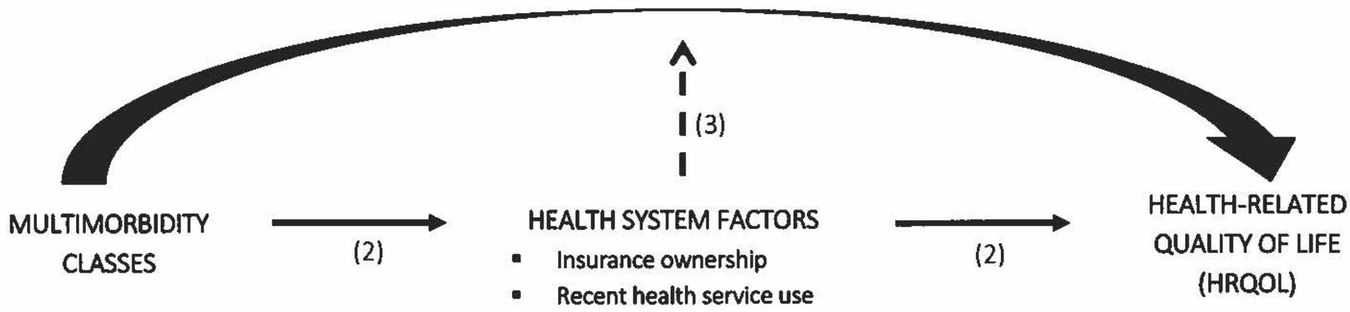

Figure 1. Conceptual framework to guide data analysis
(1) Direct effect of multimorbidity class membership on health-related quality of life (HRQoL); (2) indirect effects via health system factors; and (3) moderation effects, where health system factors modify the multimorbidity-HRQoL relationship.

Multimorbidity class membership was hypothesized to affect HRQoL both directly and indirectly, through 3 main pathways. Path 1 tests the direct association of multimorbidity class membership on HRQoL. Given evidence of a significant inverse relationship between the number of chronic conditions and quality of life related to physical health domains,[6] it was hypothesised that multimorbidity classes would be associated with lower physical functioning. Furthermore, given that some studies have reported poorer mental health functioning where 3 or more diseases co-occur, it was expected that patterns reflecting a higher degree of multimorbidity (i.e. an increased number of conditions) would be associated with lower mental health functioning.

Path 2 posits that health system factors reflecting financial access to care (i.e. insurance coverage) and health service utilization (i.e. recent health service use) operate as mediating factors, with independent effects on the multimorbidity-HRQoL relationship. Studies implicate financial burdens associated with inability to afford private insurance among the negative experiences faced by persons with multimorbidity in trying to manage their conditions.[12] It was thus hypothesized, that by minimizing financial stress and enabling better health-seeking behaviour, insurance coverage would mediate (i.e. lessen) the impact of multimorbidity on physical and mental dimensions of HRQoL. With regard to health service utilization, on the other hand, evidence from the literature suggests that the increased health care use associated with multimorbidity is often fraught with negative experiential effects, due to challenges in navigating the system, hassles with health care interaction, and reminders of the health problems faced by individuals.[11,12] It was thus hypothesized that increased health service would mediate the multimorbidity-HRQoL relationship via a negative effect on mental health functioning.

In addition, interactions between multimorbidity and health system factors were hypothesized to moderate the multimorbidity-HRQoL relationship, either by mitigating (in the case of insurance coverage) or reinforcing (in the case of health service use) its effects on health outcomes (path 3).

Methods

Data

The JHLS-II recruited a sample of 2,848 Jamaicans, between 15-74 years old of age, over a four-month period from November 2007 and March 2008.[15,18] The study employed a multi-stage cluster sampling design, with participant recruitment based on a random selection of clusters (enumeration districts) proportionate to the size of the population within the 14 parishes of Jamaica.[15] Within each cluster, a random starting point was chosen and every 10th household systematically identified, with a single individual from each household being invited to participate.[15] An interviewer-administered questionnaire was used to obtain data on demographic characteristics, medical history and health behaviours, including physical (i.e. height, body weight, hip circumference, waist circumference) and biological (i.e. blood pressure, blood glucose, total cholesterol) measurements that were made in accordance with standardized protocols.[15,18] Further details of the survey design, sampling procedures and data collection methods are provided in the technical report.[15]

Measures

This study operationalized four categories of variables:

(1) **Exposure:** Indicators of multimorbidity class membership (i.e. individual NCDs);

(2) **Outcomes of class membership:** HRQoL outcomes, relating to physical and mental domains;

(3) **Mediators of the multimorbidity-HRQoL relationship:** Health system factors reflecting financial access to care and health care utilization; and

(4) **Covariates:** Covariates reflecting socio-demographic characteristics, economic circumstances and health behaviours.

Indicators of multimorbidity class membership

Indicators of multimorbidity class membership are all fully described in Paper 1. Briefly, measurement of multimorbidity was limited to those NCDs with the greatest burden in the population (i.e. prevalence greater than or equal to 1% in each sex). Following guidance from a 2011 systematic review on multimorbidity measurement that related diseases be combined,[19] cardiovascular disease (i.e. heart disease, myocardial infarction, and circulation problems) and mental health disorders (i.e. depression, anxiety, psychosis, and other mental health problems) were grouped together to enhance data quality. Self-reported diagnosis of bronchitis/pneumonia was used as a proxy indicator of chronic obstructive pulmonary disease (COPD). The final list of 11 conditions included hypertension, obesity, hypercholesterolemia, diabetes, asthma, arthritis, cardiovascular disease, mental health disorders, COPD, stroke, and glaucoma.

Health-related Quality of Life (HRQoL)

To assess HRQoL, the JHLS-II used the SF-12 Health Survey instrument, a multipurpose short-form consisting of 12 items used to measure eight different dimensions of health:

- Physical Functioning (i.e. physical activity limitations due to health problems);
- Role Physical (i.e. limitations in usual role activities due to physical health problems);
- Bodily Pain (i.e. disruption to normal work activities due to pain);
- General Health (i.e. self-rated health);
- Vitality (i.e. energy and fatigue);
- Social Functioning (i.e. the effect of physical and/or emotional problems on social activities);
- Role Emotional (i.e. limitations in usual role activities due to emotional health problems); and
- Mental Health (i.e. psychological distress and well-being).[20]

The SF-12 provides two easily interpretable subscales, namely the Physical Component Summary (PCS-12) score and the Mental Component Summary (MCS-12) score.[20] For each subscale, scores are calculated by creating indicator variables for all but one of the response categories for each item, multiplying each indicator variable by its respective weight (i.e. a physical or mental weight, derived from the general United States population), and summing the products to determine an aggregate score.[21] The resultant summary scale score is then transformed using a norm-based standardization method, by adding a constant derived from the general United States population, to achieve a mean score of 50 and a standard deviation (SD) of 10.[21] This step allows for meaningful comparison of PCS-12 and MCS-12 scores with each other.[21] Higher scores are indicative of better health.[7] Summary scores for both the PCS-12 and MCS-12 subscales were set to missing if an individual was missing information on any one of the SF-12 items, and mean substitution for missing values used.

Health system factors

Individual-level health system factors were assessed using two dichotomous indicators of (1) insurance coverage; and (2) health service use. To assess insurance coverage, a binary indicator of private insurance ownership was created to reflect better financial access to health services. In addition, a binary indicator of public insurance ownership was created, based on whether participants had enrolled in either the NHF or JADEP, to reflect better financial access to needed medications. Timing since the respondent last had his/her blood pressure measured was used as a proxy indicator of a recent health service visit. Ideally, service use would have been operationalized using an indicator reflecting the number of visits made within a specified period, to better capture frequency of use and the increased service utilization that has come to be associated with multimorbidity. Data availability limitations precluded operationalization of such a measure, however, and recent health service use was the best proxy that could be obtained based on information captured in the JHLS-II survey. Respondents who reported that their last blood pressure measurement was less than six months ago were coded as having a recent health care visit.

Covariates

Factors noted to impact quality of life include socio-demographic characteristics, economic circumstances, and health behaviours.[6] In this study, socio-demographic characteristics included age, which was treated as a continuous variable and included all persons 15-74 years, sex (male/female), full-time employment (yes/no) and having attained at least secondary level education or higher (yes/no). To operationalize economic circumstances, principal component analysis (PCA) was used to generate a wealth index, based on responses (i.e. yes/no) to several questions on household assets (i.e. ownership of gas/electric stove, refrigerator or freezer, microwave oven, telephone, radio, television set, cable, satellite dish, bicycle, motorbike, car, computer, washing machine, sewing machine, fan, air conditioner, compact disk (CD) player, stereo equipment, record player, and video cassette recorder) and living conditions (i.e. number of members per sleeping room). The wealth variable was categorized into quintiles (i.e. poorest to wealthiest) and then dichotomized to reflect those in the top 60% vs. the bottom 40%.

Health behaviours explored in this study included tobacco smoking, alcohol use and low physical activity levels. Dichotomous indicators of tobacco smoking and alcohol use were created to reflect past or current tobacco use (yes/no) and current alcohol drinkers (yes/no), respectively. Physical activity levels were defined based on responses to the International Physical Activity Questionnaire (IPAQ)- Short Form, using scores on walking, moderate-intensity activity and vigorous-intensity activity to determine metabolic equivalent (MET) levels. Three physical activity categories were created based on established cut-offs reflecting high (i.e. ≥ 7 or more days of any combination of walking, moderate- or vigorous-intensity activities accumulating at least 3000 MET-minutes/week), moderate (i.e. ≥ 5 days of any combination of walking, moderate- or vigorous-intensity activities achieving a minimum of at least 600 MET-minutes/week) or low (i.e. no activity or some activity reported but not enough to meet moderate or high levels) levels of activity.[22] The moderate- and high-intensity categories were then collapsed and a binary indicator reflecting low (yes/no) levels physical activity created.

Statistical approach

Analyses were restricted to participants with non-missing information on the 11 NCD multimorbidity indicators. Of the 2,848 respondents who completed the survey, 311 (10.9%) were missing information on one or more of these indicators. There were no statistically significant differences between those with complete and those with missing information on the basis on sex, age or region of residence. The final analytic sample of 2,551 respondents included 790 males and 1,761 females.

Descriptive statistics were presented using means with 95% confidence intervals (for continuous variables), and proportions (for categorial variables). All analyses were weighted to account for sampling design and non-response as well as differences in the age-sex distribution of the study sample compared to the Jamaican population. Base sampling weights reflected the product of the inverse of the probability of selecting a household and the inverse of the probability of selecting a primary sampling unit, adjusted for non-response. Post-stratification weights were calculated as the number of persons in the Jamaican population between the ages of 15-74 years, represented by each individual in the sample within 5-year age-sex categories. In accordance with recommended research practice, however, regressions were unweighted.[23]

Latent class analysis (LCA)

The LCA model was used to examine variation in HRQoL outcomes across multimorbidity latent classes. LCA is a reductionist strategy that uses a person-centred approach to identify segments of the population with diverging disease profiles.[24] LCA was used to determine NCD multimorbidity patterns based on the presence/absence of 11 NCDs. This involved fitting a series of models to the data, starting with a one-class model and increasing classes in a stepwise fashion until model fit no longer significantly improved. Baseline model selection was guided by comparison of model fit statistics (i.e. likelihood-ratio G^2 statistic) and information criteria (i.e. Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), adjusted BIC) in addition to visual inspection of probability plots to evaluate the meaningfulness and distinctiveness of resultant latent class solutions.[25,26] Steps used to determine the baseline LCA model are described in greater detail in Paper 1.

Next, a Bayes' theorem-based approach was used to estimate the effect of multimorbidity class membership on HRQoL outcomes, relating to physical and mental domains. This approach involved fitting the latent class model with the outcome included as a covariate, and then using Bayes' theorem to reverse the direction of the effect and empirically derive the class-specific distribution of mean (i.e. PCS-12; MCS-12) scores, via kernel density estimation.[27] Pairwise tests and corresponding *p*-values were used to compare each multimorbidity pattern with the reference class, to test the null hypothesis that scores were equal. All statistical analyses were carried out via Stata v.15 software, using the LCA Stata Plugin[28] and the LCA_Distal_BCH Stata function[29] as needed. Statistical significance was indicated by a *p*-value < 0.05.

Regression analysis

Following LCA, individuals were assigned to their best fit class based on their maximum posterior probability. Multivariate regression methods were then used to further examine the multimorbidity-HRQoL relationship, controlling for important confounders known to affect quality of life outcomes.

Mediation Analyses

To investigate the role of the health system on HRQoL outcomes, the counterfactual approach to mediation analysis, developed by Valeri and VanderWeele[30], was used. Generally speaking, mediation models allow for investigation of the mechanisms underlying an observed relationship between an exposure variable and an outcome variable, by hypothesising involvement of a third intermediate (mediator) variable.[30] In order for a variable to be considered a mediator, certain criteria must be met, namely (1) the exposure must be significantly associated with the hypothesized mediator; (2) the mediator must be significantly associated with the outcome; (3) the exposure must be significantly associated with the outcome (although experts note that this relationship is not necessary since a statistically significant association may not be evident when direct and mediated effects have opposite signs); and (4) the exposure-outcome relationship must be attenuated after controlling for the hypothesized mediator.[30,31]

This counterfactual approach extends traditional mediation analysis, by allowing the total effect of multimorbidity on HRQoL to be decomposed into direct and indirect effects, using models with interactions (e.g. between multimorbidity classes and health system factors) and non-linearities (e.g. binary mediators such as insurance coverage and recent health service use).[30] Analyses were performed in Stata using the *paramed* program, which is based on the mediation macro developed by Valeri and VanderWeele.[30] This program requires that the exposure variable be operationalized as a binary (0/1) variable. Accordingly, the multimorbidity classes were recoded as three separate indicator variables to reflect the patterns identified (i.e. *Metabolic, Vascular-Inflammatory, Respiratory*). To satisfy identifiability assumptions regarding no confounding, specific covariates were included in the regression approach[30], to reflect socio-demographic characteristics (i.e. age, sex, education level, employment status), economic circumstances (i.e. wealth quintile), and health behaviours (e.g. current alcohol use; smoking history, physical activity level). Potential interactions between multimorbidity classes and health system factors were tested in their effects on HRQoL and included where significant. Natural direct and indirect effects were estimated by fitting a linear regression model for the continuous outcome and a logistic regression model for the binary mediator, respectively.[30] From these combined models, estimates for the natural direct effects, natural indirect effects and total effects (i.e. the sum of the natural direct and indirect effects) were determined.[30] Bias-corrected bootstrap confidence intervals were obtained via bootstrap procedures with 1000 replications. The proportion of the multimorbidity-HRQoL relationship mediated through health system factors was calculated as the ratio of the natural indirect effect to the total effect.

Results

LCA results

Fit statistics, information criteria and model interpretability together suggested that the four-class solution was the optimum baseline model. Latent class prevalences and item-response probabilities (i.e. the estimated probability of reporting a particular NCD, given membership in a particular latent class) for the four-class model are illustrated in Table 1.

Class 1 was labelled *Relatively Healthy* as it was characterized by individuals with low probabilities of all 11 NCDs. The majority of sample respondents (52.70%) was classified into this relatively healthy class where the mean number of NCDs was 0.40. *Class 2* was characterized by individuals with a high probability of hypertension and obesity, and somewhat moderate probability of hypercholesterolemia. This class was labelled *Metabolic* and comprised 30.88% of the sample. The mean number of NCDs was 1.60 and nearly one in five participants (19.80%) in this class had at least three NCDs. *Class 3* was characterized by individuals with a very high probability of hypertension, obesity, hypercholesteremia and diabetes. Specifically, members of Class 3 had a higher probability of these four NCDs than all other classes. Class 3 was also marked by an increased likelihood of arthritis and cardiovascular disease. This class was labelled *Vascular-Inflammatory* and comprised 12.21% of the sample. The mean number of NCDs was 3.40. The final class, *Class 4,* was characterized by individuals with the highest probability of asthma and COPD and was accordingly labelled *Respiratory*. This was the smallest of all classes, comprising 4.20% of the sample. The mean number of NCDs was 2.86.

Table 1. Four-Latent-Class Model of Multimorbidity (JHLS-II data, 2007/2008; N=2,551)				
	Latent Class			
	1	2	3	4
	Relatively Healthy	Metabolic	Vascular Inflammatory	Respiratory
Latent class prevalences	0.53	0.31	0.12	0.04
Item-response probabilities	Probability of a Yes response			
Hypertension	0.05	**0.58**	**0.80**	0.14
Obesity	0.20	**0.39**	**0.56**	**0.53**
Hypercholesterolemia	0.05	0.23	**0.36**	0.20
Diabetes mellitus	0.00	0.17	**0.36**	0.08
Asthma	0.07	0.02	0.06	**0.45**
Arthritis	0.03	0.04	**0.43**	0.05
Cardiovascular disease	0.02	0.00	**0.41**	0.10
Mental health disorders	0.02	0.01	0.07	0.12
COPD	0.02	0.00	0.05	**0.41**
Stroke	0.00	0.01	0.10	0.00
Glaucoma	0.00	0.02	0.07	0.00
Multimorbidity (2+ NCDs)	4.66	63.60	100.00	100.00
Multimorbidity (3+ NCDs)	0.20	19.80	84.65	59.65
Mean number of NCDs reported (95% CI)	0.40 (0.36, 0.45)	1.60 (1.53, 1.67)	3.40 (3.23, 3.56)	2.86 (2.72, 3.00)

*Item-response probabilities ≥0.35 in boldface to facilitate interpretation

Insurance coverage

A significantly larger proportion of the sample had private insurance (18.84%) compared to public insurance coverage (p=0.02) (Figure 2). Different patterns emerged across multimorbidity classes, however, with the *Metabolic* class less likely (p=0.033) and the *Vascular-Inflammatory* class (p=0.003) more likely to own private insurance than their *Relatively Healthy* counterparts. On the other hand, with regard to public insurance coverage, all multimorbidity classes were significantly more likely to be enrolled in either of the government subsidized programs ($p<0.0001$).

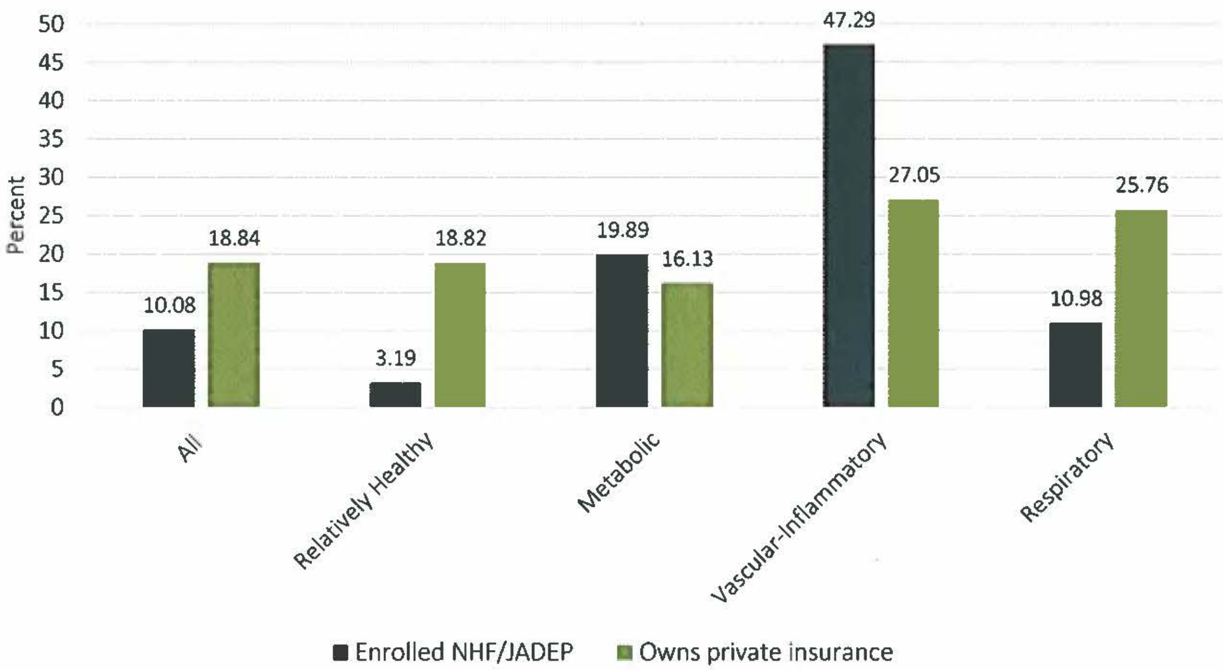

Figure 2. Insurance coverage, according to class membership

Distribution of mean HRQoL subscale scores

Mean PCS-12 and MCS-12 scores for the survey population were 51.25 (SD=8.54) and 49.47 (SD=9.03), respectively. Participants generally scored lower on the MCS-12 scale compared to the PCS-12 scale. With successive age-groupings, participants scored lower on the PCS-12 scale ($p<0.001$) but higher on the MCS-12 scale ($p<0.01$) (Figure 3).

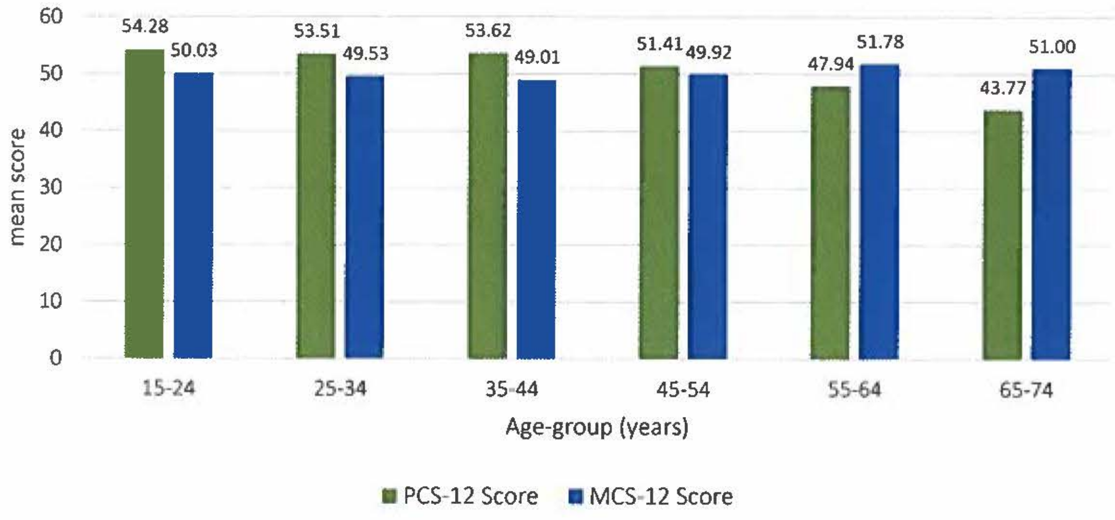

Figure 3. Distribution of mean PCS-12 and MCS-12 subscale scores, according to age-group (JHLS-II data, 2007/2008; N=2,551)

Table 2 presents mean PCS-12 and mean MCS-12 scores, given latent class membership. Individuals in the *Metabolic* and *Vascular-Inflammatory* classes scored 2.72 (p<0.001) and 13.37 (p<0.001) points lower on the PCS-12 subscale, respectively, that their *Relatively Healthy* counterparts. There were no statistically significant differences in mental health functioning scores according to latent class membership.

Table 2. Mean HRQoL subscale scores, according to latent class (JHLS-II data, 2007/2008; N=2,551)

	Physical Component Summary (PCS-12) score			Mental Component Summary (MCS-12) score		
Latent Class	Mean score	95% CI	*p*-value	Mean score	95% CI	*p*-value
Relatively Healthy	53.85	(53.37, 54.33)	[ref]	49.56	(48.94, 50.19)	[ref]
Metabolic	51.13	(50.13, 52.12)	<0.001	50.49	(49.50, 51.48)	0.179
Vascular-Inflammatory	40.48	(38.64, 42.32)	<0.001	48.56	(47.07, 50.05)	0.211
Respiratory	52.56	(49.46, 55.65)	0.435	45.62	(41.49, 49.75)	0.074

p-values based on Wald chi-squared tests

Multivariate regression analyses

Following assignment of individuals to their best fit class based on their maximum posterior probability, regression estimates indicated that, compared to those in the *Relatively Healthy* class, membership in the *Vascular-Inflammatory* class (β=-5.48; *p*<0.001) was associated with significantly lower PCS-12 scores (Table 3). With regard to MCS-12 scores, individuals in the both *Vascular-Inflammatory* class (β=-1.69; *p*<0.05) and *Respiratory* class (β=-2.53; *p*<0.05) scored substantially lower that their *Relatively Healthy* counterparts.

Table 3. Multivariate regression analysis of effect of multimorbidity class membership on HRQoL outcomes (JHLS-II data, 2007/2008; N=2,551)

	Physical Component Summary score (PCS-12)	Mental Component Summary score (MCS-12)
	β (95% CI)	β (95% CI)
Multimorbidity class		
Relatively healthy	[ref]	[ref]
Metabolic	-0.13 (-0.89,0.62)	-0.27 (-1.16,0.63)
Vascular-Inflammatory	-5.48*** (-6.66,-4.29)	-1.69* (-3.09,-0.28)
Respiratory	-0.35 (-2.41,1.70)	-2.53* (-4.97,-0.09)
Age, years	-0.11*** (-0.14,-0.09)	0.06*** (0.03,0.09)
Female sex	-0.26 (-0.99,0.48)	-2.60*** (-3.47,-1.73)
Secondary level or higher	1.39*** (0.64,2.15)	-0.67 (-1.57,0.23)
Employed full-time	1.46*** (0.84,2.07)	0.21 (-0.53,0.94)
Top 60% wealth quintile	0.51 (-0.13,1.16)	1.42*** (0.66,2.19)
Currently use alcohol	0.66* (0.00,1.32)	-0.76 (-1.55,0.02)
Past or present smoker	-0.39 (-1.10,0.33)	-1.88*** (-2.73,-1.03)
Low levels of physical activity	-0.93** (-1.53,-0.32)	-0.55 (-1.27,0.17)
Private insurance coverage	-0.18 (-1.00,0.65)	1.11* (0.14,2.09)
Public insurance coverage	-2.69*** (-3.66,-1.73)	0.17 (-0.97,1.31)
Recent health service use	-0.53 (-1.18,0.11)	-1.03** (-1.80,-0.27)

CI = confidence interval
Estimates based on non-missing data (<1% missing across all variables)
*p<0.05; **p<0.01; ***p<0.001

Results of the multivariate model also indicated that advancing age was associated with lower PCS-12 scores (β=-0.11; p<0.001), but higher MCS-12 scores (β=0.06; p<0.001). Higher educational attainment (β=1.39; p<0.001) and full-time employment (β=1.46; p<0.001) were associated with higher PCS-12 scores, while low levels of physical activity (β=-0.93; p<0.01) were associated with lower PCS-12 scores. For mental health functioning, being in the top 60% wealth quintile (β=1.23; p<0.001) was associated with higher MCS-12 scores. Conversely, being female (β=-2.60; p<0.001) and self-reporting past of current use of tobacco (β=-1.88; p<0.001) were associated with lower MCS-12 scores. Public insurance coverage was associated with lower PCS-12 scores (β=-2.69; p<0.001) while private insurance coverage was associated with higher MCS-12 scores (β=1.11; p<0.05). Recent health service use was associated with lower scores on the MCS-12 subscale (β=-1.03; p<0.01).

Mediation analyses

Results of the mediation analyses for PCS-12 and MCS-12 scores are presented in Tables 4 and 5, respectively. As noted above, significant total effects were observed between the *Vascular-Inflammatory* class and PCS-12 scores, while lower MCS-12 scores were significantly associated with membership in both the *Vascular-Inflammatory* and *Respiratory* classes (Table 3).

There was some mediation by public insurance coverage (Table 4), with 4.77% of the total effect of the *Vascular-Inflammatory* class on PCS-12 scores mediated by enrolment in government subsidized programs (β_{total}=-5.66, p<0.001; $\beta_{indirect}$ =-0.27, p<0.01). There was no statistically significant indirect effect mediated by recent service use or private insurance coverage.

Table 4. Mediation Analysis: Effects of multimorbidity on the PCS-12 subscale scores			
	Natural direct effect	Natural indirect effect	Marginal total effect
	β (95% CI†)	β (95% CI†)	β (95% CI†)
Vascular-Inflammatory class			
Mediator: Recent service use[a¥]	-5.38*** (-6.80, -3.98)	-0.17 (-0.26, 0.02)	-5.49*** (-6.93, -4.15)
Mediator: Private insurance[b]	-5.66*** (-7.17, -4.24)	0.16 (-0.05, 0.57)	--5.50*** (-6.93, -4.08)
Mediator: Public insurance[c¥]	-5.38*** (-6.73, -3.86)	-0.27** (-0.53, -0.14)	-5.66*** (-7.03, -4.17)

PCS-12 = Physical Component Summary Score

† bias-corrected confidence interval

¥ The exposure-mediator interaction was not significant at the $p<0.05$ level and not included in the model

[a] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, insurance coverage

[b] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, public insurance coverage recent service use

[c] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, private insurance coverage recent service use

With regard to mental health outcomes, the total effects of the *Vascular-Inflammatory* class and the *Respiratory* class on MCS-12 scores both appeared to be mediated by recent health service use (Table 5). The proportions mediated through recent service use were 13.25% and 10.04%, for the association between MCS-12 scores and membership in the *Vascular-Inflammatory* class (β_{total}=-1.66, $p<0.05$; $\beta_{indirect}$=-0.22; $p<0.05$) and the *Respiratory* class (β_{total}=-2.49, $p<0.05$; $\beta_{indirect}$=-0.25; $p<0.05$), respectively. There was no statistically significant indirect effects on MCS-12 scores by insurance coverage for either the *Vascular-Inflammatory* or *Respiratory* classes.

Table 5. Mediation Analysis: Effects of multimorbidity on the MCS-12 subscale scores			
	Natural direct effect	Natural indirect effect	Marginal total effect
	β (95% CI†)	β (95% CI†)	β (95% CI†)
Vascular-Inflammatory class			
Mediator: Recent service use[a¥]	-1.44* (-2.85, -0.11)	-0.22* (-0.42, -0.08)	-1.66* (-3.01, -0.37)
Mediator: Private insurance[b¥]	-1.44* (-3.00, -0.19)	0.09 (0.02, 0.25)	-1.35* (-2.90, -0.09)
Mediator: Public insurance[c¥]	-1.44* (-2.82, -0.11)	0.01 (-0.10, 0.15)	-1.42* (-2.75, -0.13)
Respiratory class			
Mediator: Recent service use[a¥]	-2.24 (-5.48, 0.55)	-0.25* (-5.39, -0.06)	-2.49* (-5.57, 0.33)
Mediator: Private insurance[b¥]	-2.24 (-5.44, 0.51)	-0.02 (-0.12, 0.06)	-2.25 (-5.48, 0.43)
Mediator: Public insurance[c]	-2.10 (-6.24, 1.48)	-0.38 (-2.65, 1.45)	-2.48 (-5.52, 0.63)

MCS-12 = Mental Component Summary Score

† bias-corrected confidence interval

¥ Exposure-mediator interactions were not significant at the $p<0.05$ level and not included in the models

[a] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, private insurance coverage

[b] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, public insurance coverage recent service use

[c] Adjusted for age, sex, education, employment, wealth, current alcohol use, past or present smoking status, physical activity level, private insurance coverage recent service use

Discussion

This study used LCA to explore the distribution of HRQoL outcomes conditional on latent class membership. Findings indicate that beyond the accumulation of an increasing *number* of conditions, risk of adverse HRQoL outcomes is further modified by the *types* of disease combinations. Specifically, the study illustrated that specific disease profiles are differentially associated with poorer physical functioning, with the *Metabolic* class and the *Vascular-Inflammatory* class scoring 2.73 ($p<0.001$) and 13.37 ($p<0.001$) points lower, respectively, than their counterparts in the *Relatively Healthy* class. After controlling for important confounders, results continued to implicate multimorbidity patterns as important predictors of physical functioning and well-being, with membership in the *Vascular-Inflammatory* class associated with lower PCS-12 scores, compared to membership in the *Relatively Healthy* class. With regard to mental health functioning, results of the multivariate regression analyses indicated that multimorbidity patterns were also important predictors of psychological well-being, with significant inverse relationships observed between MCS-12 scores and membership in both the *Vascular-Inflammatory* and *Respiratory* classes.

In considering entry points for intervention, to support improved management of conditions through better physical functioning and emotional wellbeing, results of mediation analyses highlight possible pathways, namely via financial access to care and use of health services. Specifically, there was a significant mediated effect through recent health service, on the relationship between multimorbidity and mental health functioning, for individuals in both the *Vascular-Inflammatory* and *Respiratory* classes. This finding corroborated the hypothesis that health care use would mediate the multimorbidity-HRQoL association via a negative effect, reflecting personal frustrations and health system hassles that have been reported in the international literature among primary care patients with prevalent multimorbidity. A small, yet statistically significant mediated effect through public insurance coverage was also observed, indicating that enrolment in either the NHF or JADEP was associated with lower physical functioning. This finding may reflect a limitation of cross-sectional analyses which challenge temporal ordering of exposure and outcome, as it is not clear why access to medications would be associated with lower physical functioning. One possible explanation lies in the nature of these government subsidized programs, where the JADEP caters to populations over the age of 60 years (where physical limitations are more common) while the NHF is a needs-based program with enrolment conditional on the confirmed diagnosis of disease. It is thus likely that persons seek the benefits of these programs after their illnesses have reached a more advanced stage where physical limitations become apparent and pharmaceutical intervention is more urgent. Regardless, this finding underscores the need for timely access to services and medications to better support the management of multiple co-existing morbidities and prevent the accumulation of new ones.

Generally speaking, findings from this study are consistent with evidence of the negative impact of an increasing number of diseases on HRQoL outcomes, with results indicating an increased vulnerability of members in the *Vascular-Inflammatory* class to poor quality of life outcomes, across both physical and mental domains. In this study, the *Vascular-Inflammatory* class was characterized by a very high probability of hypertension, obesity, hypercholesteremia and diabetes, in addition to an increased likelihood of self-reported arthritis and cardiovascular disease. Results are thus in keeping with evidence from a systematic review indicating a significant inverse relationship between increasing number of chronic conditions and HRQoL outcomes, relating to physical dimensions of health.[6] Interestingly, rather than use simple disease counts, one study among 238 primary care patients (18 years or older) in Saguenay region, Canada, explored differential impacts on HRQoL in association with varying combinations of conditions grouped by anatomical domain.[10] Similar to findings from this study of a significant inverse relationship between PCS-12 scores and the *Vascular-Inflammatory* pattern, this Canadian study concluded that vascular, upper gastro-intestinal and musculoskeletal systems have strong negative effects on physical dimensions of HRQoL.[10] Given that the PCS-12 subscale is heavily weighted towards HRQoL aspects reflecting physical functioning, general health and pain, these findings suggest that interventions targeting physical therapy and pain management may promote better disease control and quality of life outcomes for members of the *Vascular-Inflammatory* class.

Further, while evidence on the effect of the number of chronic diseases on mental health aspects of HRQoL is less clear, some investigators have reported an impact with 3 or more diagnoses.[6] Notably, the mean number of NCDs reported among members of the *Vascular-Inflammatory* and *Respiratory* classes was 3.40 and 2.86, respectively, consistent with evidence of an effect of multimorbidity on mental health domains in patients with 3 or more diagnoses.[6] The MCS-12 subscale is heavily weighted towards HRQoL aspects reflecting vitality, social engagement, emotional health and psychological distress. More investigation is needed to understand how *Vascular-Inflammatory* and *Respiratory* patterns differentially affect energy levels, social functioning and mental well-being to support more holistic care interventions and improved outcomes. Given that individuals in the *Vascular-Inflammatory* class appear to be at greatest risk for poor physical and mental health functioning, further investigation into the role of health system factors in reinforcing or mitigating poor outcomes is also warranted. Chronicity of NCDs and the dynamic nature of health and well-being predispose these individuals to negative feedback cycles, where poorer quality of life outcomes reduce capacity to manage multiple conditions and facilitate the accumulation of new ones.[8] Minimizing risk of adverse health outcomes in this vulnerable sub-population requires a deeper look into health-seeking behaviours, coping strategies and the role of enabling factors (e.g. insurance) in alleviating concerns regarding access to and use of care. Anecdotal reports suggest that public health clinics in Jamaica are typically overburdened with serving large numbers of the population, such that clients experience difficulty scheduling appointments outside of a usual 3-6-month window in addition to challenges concerning the inconsistent availability of drug availability and limited surgical intervention with the public domain. Future qualitative work would allow for better elaboration of the subjective experiences of Jamaicans with prevalent multimorbidity, as well as challenges and concerns regarding financial access to services and medication.

Strengths & limitations

The study has several limitations. First of all, the cross-sectional nature of the study challenges the assumption of temporal ordering needed for mediation analysis, which requires that the exposure (i.e. multimorbidity) preceded the mediator (i.e. health system factors) which, in turn, preceded the outcome (i.e. scores on the HRQoL subscales).

Secondly, although maximum probability assignment techniques have been widely used throughout the literature to estimate the associations between latent class membership and distal outcomes, these approaches fail to account for uncertainty in class membership.[27] Further, simulation studies comparing contemporary model based approaches using Bayes' theorem to more traditional approaches such as maximum probability assignment, indicate that the latter technique often attenuates effects of the exposure on the outcome[27] – suggesting that the impact of multimorbidity patterns on HRQoL outcomes may be even greater than estimated here. Given that the Bayes' theorem based approach is recommended as a more robust technique for modelling the effect of latent classes on a distal outcome,[27] use of this approach to examine the distribution of mean PCS-12 and MCS-12 scores, conditional on class membership, is noted as a strength of this study. Unfortunately, this model does not allow for statistical control of potential confounders or formal tests of mediation. Although the maximum probability assignment method has been noted to produce less biased estimates compared to other classify-analyze approaches,[27] limitations of this technique must be borne in mind in interpretation of the results.

There are also limitations in measurement of various indicators used in this study, including the definition and measurement of potential mediators, such as health service utilization. As noted earlier, the recent service use variable was a convenience measure, with selection based on what was available from the JHLS-II questionnaire. Limitations of this binary indicator are acknowledged, including failure to capture the type of health care service used (e.g. primary, secondary, tertiary) and the purpose of the visit (i.e. routine vs. emergency consultation) or the number of health visits made with a given time period. Furthermore, despite inclusion of several covariates deemed relevant, residual confounding due to omission of potentially important factors (e.g. social support; severity of diseases, number of medications being used) is acknowledged. Studies note that important factors impacting the multimorbidity-HRQoL relationship may include the presence of coexisting acute conditions, time since diagnosis of chronic diseases, and the prognosis of health conditions.[6] This limitation could have potentially biased the natural direct and indirect effect estimates observed here.

Conclusion

This study identified differential effects of specific combinations of diseases on HRQoL outcomes, demonstrating the clinical utility and predictive validity of latent classes (i.e. multimorbidity patterns) in estimating risk of poor functioning and well-being across physical and mental dimensions of health. In order to better tailor interventions to support management of multiple conditions, additional research is needed to further elaborate personal experiences with healthcare and examine how health system factors reinforce and/or mitigate positive health-seeking behaviours, including timely use of health services.

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