

Sex-Specific Multimorbidity Patterns Identified by Latent Class Analysis in the UK Alzheimer’s Disease Research Center Cohort

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Introduction

- Multimorbidity, defined as the presence of 2 or more chronic conditions, is highly prevalent in older adults and is associated with adverse cognitive and functional outcomes.
- Chronic conditions often cluster in distinct patterns.
- Emerging evidence suggests that multimorbidity may contribute to cognitive aging through sex-specific mechanisms.
- However, whether multimorbidity profiles differ between males and females remains poorly understood.

OBJECTIVE:

- To identify sex-specific multimorbidity phenotypes among older adults enrolled in the University of Kentucky Alzheimer's Disease Research Center using latent class analysis.

Results

PARTICIPANT CHARACTERISTICS:

- Participant characteristics are summarized in Table 1.

LATENT CLASS ANALYSIS FINDINGS (Figure 1, Table 2):

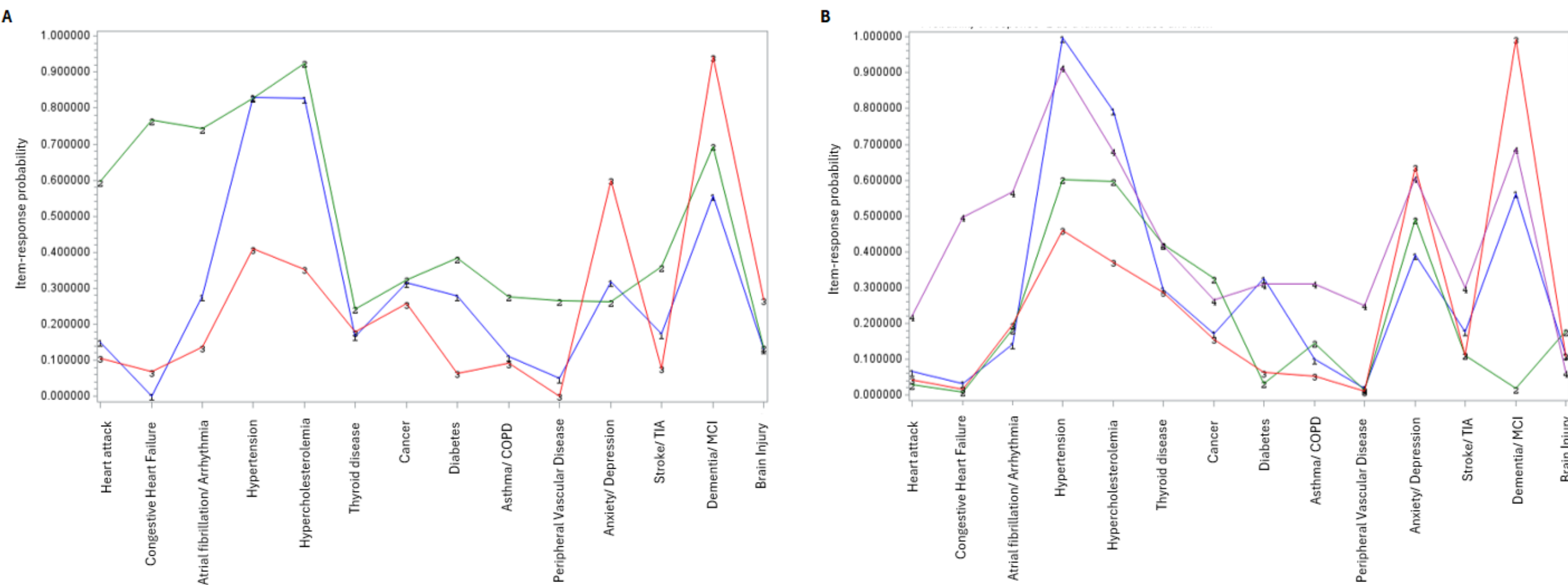
MALES (n=627):

- A three-class solution provided the best model fit.
- Cardiometabolic aging phenotype (72%).
- Neurocognitive and mental health phenotype (21%).
- Severe cardiovascular burden phenotype (7%).

FEMALES (n=963):

- A four-class solution provided the best model fit.
- Cardiometabolic burden with cognitive vulnerability phenotype (40%).
- Mental health and endocrine phenotype (25%).
- Neurocognitive and mental health phenotype (25%).
- High multisystem burden phenotype (10%).

Figure 1. Sex-Specific Multimorbidity Phenotypes in A) Males, and B) Females



Note: Males-Class 1: cardiometabolic aging predominant; 2: severe cardiovascular burden; 3: neurocognitive and mental health predominant. Females-Class 1: cardiometabolic burden with cognitive vulnerability; 2: mental health - endocrine predominant; 3: neurocognitive - mental health predominant; 4: high multisystem burden.

Methods

STUDY POPULATION:

- Community-based cohort of adults aged ≥ 50 years enrolled in the University of Kentucky Alzheimer's Disease Research Center.
- Included participants with multimorbidity, defined as ≥ 2 chronic conditions.

MEASURES:

- Fourteen chronic conditions spanning cardiovascular, metabolic, respiratory, neurologic, and mental health domains
- Cognitive status classified as cognitively normal, mild cognitive impairment (MCI), or dementia.

STATISTICAL ANALYSIS:

- Latent class analysis (LCA) was performed separately in males and females
- For each sex, LCA models with 2-6 latent classes were evaluated.
- Model selection was based on adjusted Bayesian Information Criterion (aBIC), entropy, parsimony, and clinical interpretability.
- Item-response probabilities were used to characterize multimorbidity phenotypes

Table 1. Participant characteristics, n=1,590

Age, mean (SD), yrs	79.4 (8.5)
Female	61%
MMSE, mean (SD)	23.6 (8.4)
MCI	20%
Dementia	37%
Number of chronic conditions, mean (SD)	4.0 (1.6)

Conclusions

- Sex-specific multimorbidity phenotypes were identified in this aging cohort.
- Women exhibited greater multimorbidity heterogeneity and distinct mental health, and endocrine-related profiles.
- Sex-specific disease clustering may contribute to different pathways of cognitive aging and dementia risk.

Table 2. Key Chronic Conditions by Latent Class, Stratified by Sex

Sex	Class	Gamma estimates* (by sex)	Selected high-probability conditions
Male	1: cardiometabolic aging predominant	0.68	Hypertension, hypercholesterolemia, cancer, dementia or MCI
	2: severe cardiovascular burden	0.08	Heart attack, congestive heart failure, atrial fibrillation or arrhythmia, diabetes
	3: neurocognitive and mental health predominant	0.24	Dementia or MCI, anxiety or depression
Female	1: cardiometabolic burden with cognitive vulnerability	0.37	Hypertension, hypercholesterolemia, dementia/MCI
	2: mental health - endocrine predominant	0.25	Anxiety or depression, thyroid disease, hypertension, hypercholesterolemia
	3: neurocognitive - mental health predominant	0.26	Dementia or MCI, anxiety/depression
	4: high multisystem burden	0.12	Congestive heart failure, atrial fibrillation/arrhythmia, hypertension

*Class membership probabilities; MCI- mild cognitive impairment.

References

- Abad-Díez, José María, et al. BMC geriatrics 14.1 (2014): 75.
- Agur, Karolina, et al. Int. J. Environ. Res. Public Health 13.4 (2016): 391.

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