

Analyzing Multimorbidity Patterns & Sepsis Outcomes in Critical Care: A Replication Study Using Latent Class Analysis on the MIMIC-III Dataset

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Abstract

Each year, 11 million people die from Sepsis: that is 1 in 5 deaths globally. With this in mind, Sepsis has maintained its position as one of the most complex and deadly conditions in intensive care units, where patient outcomes are not only determined by their current physiological state, but are confounded by their underlying chronic diseases. Previous research by Zador et al. (2019) proposed that these combinations of chronic illnesses can be patterned into distinct patient subgroups that differ in risk of organ failure and mortality.

In this project, we attempt to replicate the study's methodology and findings using the same MIMIC-III database. We establish our data processing pipelines with SQL, apply Elixhauser comorbidity groupings, and perform Latent Class Analysis (LCA) to identify clinically meaningful subpopulations within the ICU cohort. By revisiting this influential study, we strive to strengthen the evidence base for integrating chronic disease patterns into Sepsis prognosis and critical care decision-making.

Code: <https://github.com/kshannon-ucsd/25fa-dsc180a-team2.git>

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1 Introduction

1.1 Intro

Our goal for Quarter 1 of the capstone project is to reproduce the findings of the study using the publicly available MIMIC-III database. The aim of reproducing a paper's results is to affirm the original authors' findings and methodologies. This process is vital in science to ensure results are robust and reliable, not merely due to chance or analytical bias. By reproducing this study, we seek to validate the reported identification of distinct multimorbidity subgroups among ICU patients and their differing risks for sepsis, organ failure, and mortality.

1.2 Literature Review

We want to reproduce the results from *Multimorbidity states associated with higher mortality rates in organ dysfunction and sepsis: a data-driven analysis in critical care*. Research establishes that the underlying burden of chronic disease significantly influences the outcomes in critical illness: for example, epidemiologic analyses showed that comorbidities nearly double the risk of mortality in sepsis populations. Studies of multimorbidity in general populations further show that multiple chronic conditions are associated with greater healthcare utilization, worse quality of life, and higher mortality. Traditional ICU risk-scoring systems such as SAPS II, SOFA, and OASIS focus largely on physiologic derangement within 24 h of admission and incorporate limited or no explicit modelling of multimorbidity beyond a few chronic health items. In response, the paper incorporates clustering and latent class methods to build heterogeneous critical-care cohorts in order to better capture unobserved patient subgroups. Researchers apply latent class analysis to the large, publicly available MIMIC-III dataset with Elixhauser-defined morbidities to identify six discrete multimorbidity subgroups and then demonstrate that these are differentially at risk for organ dysfunction, sepsis, and death. It moves beyond simply counting comorbidities to mapping disease-co-occurrence patterns and their association with critical-illness trajectories, thereby filling a gap in the literature about how distinct morbidity profiles (rather than single morbidities) are linked to adverse critical care outcomes.

1.3 Relevant Data

We are incorporating the same database used by the researchers in the paper, an open-source Medical Information Mart for Intensive Care III (MIMIC III) database. It is a large de-identified health-related dataset from Beth Israel Deaconess Medical Center, comprising records of over 40,000 patients' stays in critical care units between 2001 and 2012. From the database, we want to recreate the same dataset that focuses specifically on adult patients (≥ 16 years old), after excluding those with missing demographic data, implausible or extreme physiological values, or incomplete diagnostic coding. Each patient's comorbid-

ity profile was derived from the International Classification of Diseases (ICD-9) diagnostic codes available in the database. Using the Elixhauser Comorbidity Index, which classifies 30 chronic disease categories. The authors built a binary patient-by-comorbidity matrix indicating the presence or absence of each condition per individual. This structured comorbidity data, combined with demographic information (age, sex, ethnicity) and hospital outcomes (mortality, length of stay, organ failure, and sepsis occurrence), formed the analytic dataset.

2 Methods

2.1 Data Source and Cohort Construction

All analyses were conducted using the Medical Information Mart for Intensive Care III (MIMIC-III) database, a large, de-identified ICU dataset containing detailed clinical records for over 40,000 adult patients admitted to Beth Israel Deaconess Medical Center between 2001 and 2012 [Zador et al. \(2019\)](#).

To mirror the original study, we restricted the cohort to first ICU admissions for adult patients aged ≥ 16 years. We excluded encounters with missing demographic data, implausible physiological values, or incomplete diagnostic coding. Using the DIAGNOSES_ICD table, we extracted all ICD-9 diagnosis codes and linked them to patient-level demographic and hospitalization information (age, sex, ethnicity, admission type, ICU and hospital mortality).

2.2 Comorbidity Mapping and Feature Construction

Chronic disease burden was encoded using the Elixhauser Comorbidity Index, which groups ICD-9 diagnosis codes into 30 mutually exclusive chronic-disease categories. We implemented the same mapping logic as in the publicly available MIMIC-III code repository to ensure consistency with the definitions used by [Zador et al. \(2019\)](#).

For each patient, we constructed a binary indicator vector specifying the presence or absence of each Elixhauser category. Together with age and admission type (elective vs. non-elective), these indicators formed the feature set for latent class analysis. Additional outcome variables (sepsis status, organ dysfunction, Sequential Organ Failure Assessment (SOFA) scores, and in-hospital mortality) were retained for downstream subgroup characterization but were not used as inputs to the clustering model.

2.3 Reproduction of Descriptive Analyses

Before performing latent class analysis, we reproduced the descriptive analyses presented in the original paper to validate that our reconstructed cohort matched the published pop-

ulation. Specifically, we:

- computed the prevalence of multimorbidity (two or more Elixhauser conditions) across age brackets to replicate the age-by-m multimorbidity curve (Figure 1a),
- calculated age-stratified prevalence of each Elixhauser category to generate an age-by-morbidity heatmap (Figure 1b),
- built a global disease co-occurrence network in which nodes represent comorbidities and edges represent pairwise relative risk exceeding a predefined significance threshold (Figure 1c).

These steps allowed us to confirm that the marginal distributions of age, disease burden, and morbidity composition in our cohort fell within the ranges reported by [Zador et al. \(2019\)](#).

2.4 Latent Class Analysis

To identify distinct multimorbidity subgroups within the ICU cohort, we applied Latent Class Analysis (LCA) to the patient-by-feature matrix. The manifest variables included:

- the 30 binary Elixhauser comorbidity indicators,
- age (treated as a continuous covariate),
- admission type (elective vs. non-elective).

We fit a series of LCA models with $K \in \{5, 6, 7\}$ classes. Model selection was guided by a combination of Bayesian Information Criterion (BIC), Akaike Information Criterion (AIC), and practical constraints on minimum class size. Following the approach described in [Zador et al. \(2019\)](#), we required that no latent class comprise less than 5% of the total cohort to maintain clinical interpretability.

The six-class solution achieved a favorable balance between statistical fit and parsimony and yielded clinically coherent subgroups aligned with those reported in the original study. Each patient was assigned to the class with the highest posterior membership probability.

2.5 Subgroup Characterization and Outcome Comparison

After assigning class membership, we summarized each latent subgroup in terms of:

- distribution of multimorbidity counts (number of comorbid conditions),
- age distribution,
- prevalence of each Elixhauser comorbidity,
- SOFA and OASIS scores,
- prevalence of organ dysfunction, sepsis, and in-hospital mortality.

We reproduced the original figures by generating balloon plots and boxplots for morbidity burden and age (analogous to Figures 2a and 2b), as well as circular barplots for subgroup-specific morbidity prevalence patterns (analogous to Figures 3a and 3b). These visualizations allowed direct comparison between our replicated subgroups and those identified by

Zador et al. (2019) in terms of both chronic disease profiles and associated ICU outcomes.

2.6 Network Analysis of Disease Co-Occurrence Within Subgroups

To further interrogate the internal structure of each high-risk multimorbidity subgroup, we constructed subgroup-specific disease networks. In these networks, nodes represent Elixhauser comorbidity categories, with node size proportional to prevalence within the subgroup, while edges encode the number of patients exhibiting each disease pair, normalized by the total subgroup size.

Consistent with the methodology described by Zador et al. (2019), we did not use relative risk for these within-subgroup networks, as relative risk can underestimate associations between highly prevalent conditions. Instead, raw normalized co-occurrence counts were used to highlight dominant combinations such as cardiopulmonary disease clusters, hepatic/addiction profiles, and diabetic nephropathy with hypertension. The resulting visualizations closely mirror the network structures presented in Figures 5a–5d of the original paper.

3 Results

We successfully reproduced all major findings from Zador et al. (2019), referencing MIT mimic-code to extract data cohort and creating Python/R data-processing pipeline code. Across all replicated figures, our visualizations follow the structure, scale, and analytical intent of the original paper while maintaining accuracy to the underlying MIMIC-III cohort. Below, we describe each replication figure and explain how our computational workflow captures the same clinical insights as the published analyses.

3.1 Figure 1a Replication

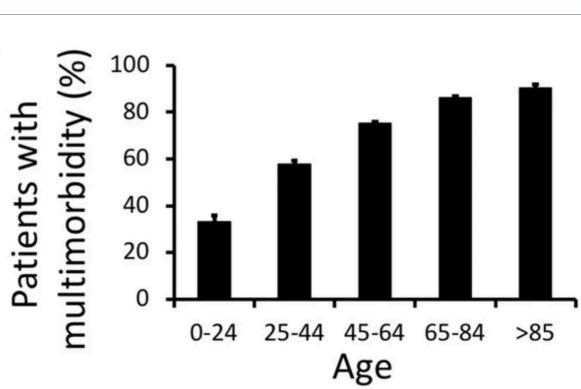
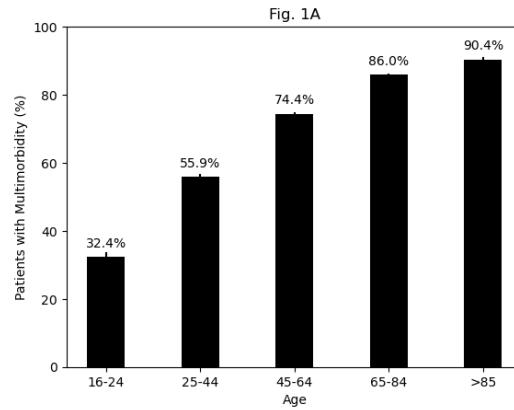


Figure 1a: (Left) Paper Figure 1a



(Right) Our replication of Figure 1a.

In the original study, Figure 1a illustrates the monotonic increase in multimorbidity prevalence with advancing age. Our replication (right panel) mirrors this relationship: the proportion of patients with two or more chronic conditions increases steadily from the youngest cohort to those above 85 years old. With each age group's percentage of multimorbidity falls in the 95 % of confidence interval.

3.2 Figure 1b Replication

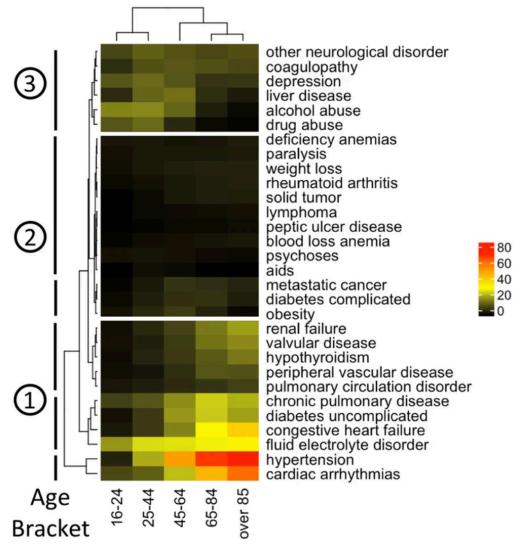
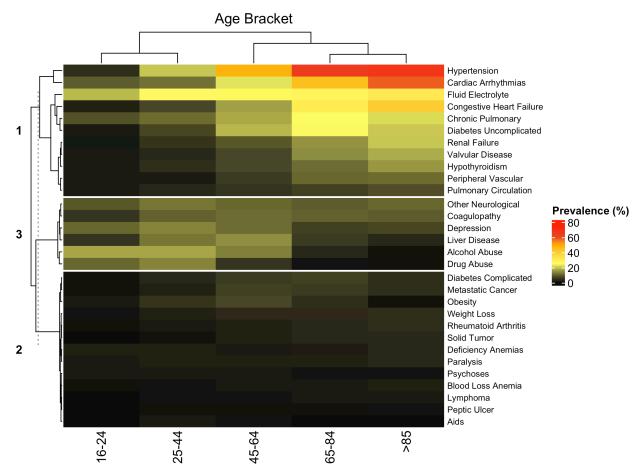


Figure 1b: (Left) Paper Figure 1b



(Right) Our replication of Figure 1b.

Despite minor differences in row ordering due to hierarchical clustering, our heatmap accurately reproduces these three canonical patterns. The smooth color gradients across age brackets, the clustering structure, and the relative intensity of age-associated conditions (e.g., cardiac, pulmonary, renal) match the qualitative findings from the original figure.

3.3 Figure 1c Replication

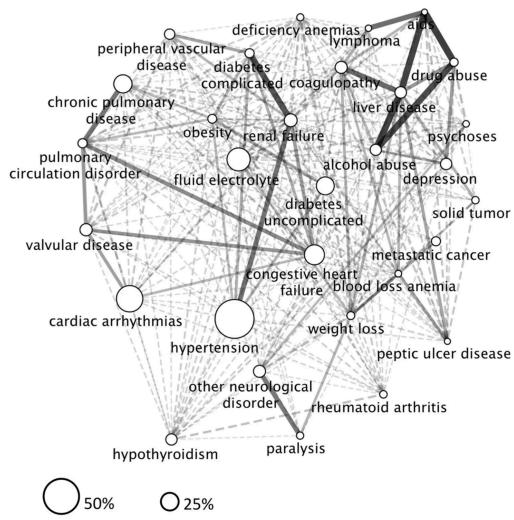
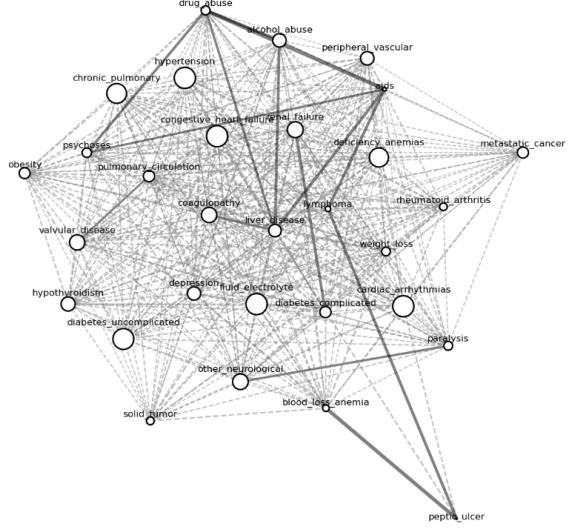


Figure 1c: (Left) Paper Figure 1c



(Right) Our replication of Figure 1c.

The network visualization in Figure 1c illustrates co-occurring morbidities in the entire study population, with node size encoding prevalence and edge width encoding relative risk between disease pairs. Our replicated graph reflects the same clinically intuitive clusters emphasized in the paper: strong co-occurrence between cardiopulmonary diseases, between diabetes and renal failure, and between alcohol/drug use disorders and liver disease.

3.4 Figure 2a Replication

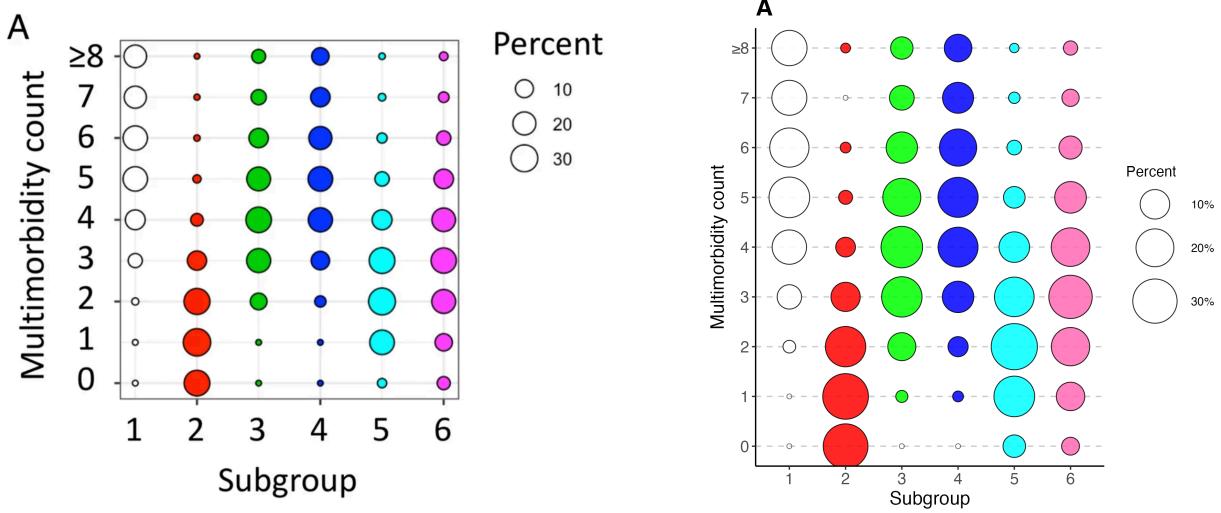


Figure 2a: (Left) Paper Figure 2a

(Right) Our replication of Figure 2a.

Figure 2a presents a balloon plot summarizing the distribution of multimorbidity counts within the six latent classes. Our replicated figure closely resembles the original: the relative sizes of the balloons within each subgroup match the patterns reported in the paper, with subgroups 1, 3, 4, and 6 exhibiting the highest multimorbidity burden.

3.5 Figure 2b Replication

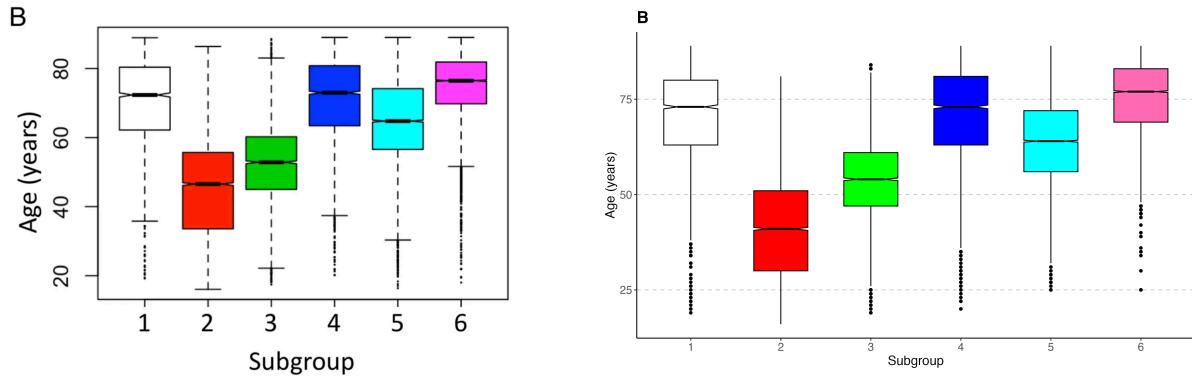


Figure 2b: (Left) Paper Figure 2b

(Right) Our replication of Figure 2b.

Our boxplot replication of Figure 2b demonstrates that our LCA-derived subgroups not only match the morbidity compositions but also recover the same age distributions reported in the original study. Subgroups with cardiopulmonary or cardiac disease burden skew older, whereas the hepatic/addiction subgroup centers on middle age, and the “young and healthy” subgroup remains markedly younger than the others.

3.6 Figure 3a Replication

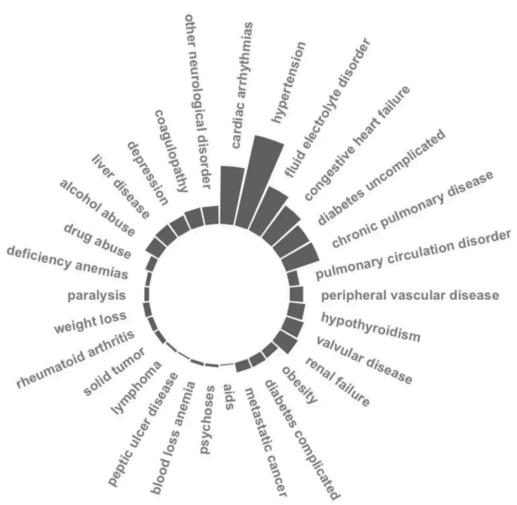
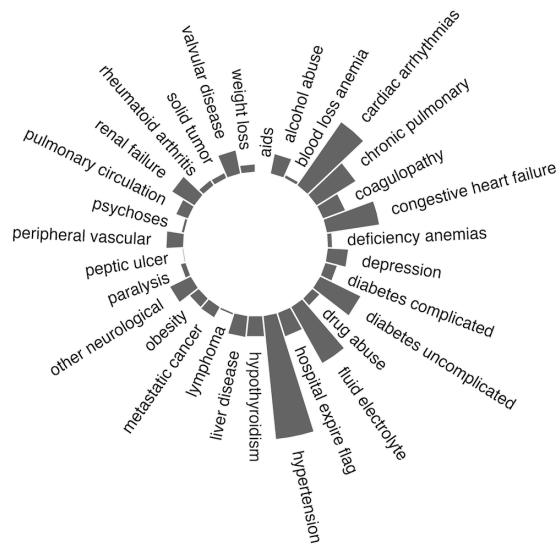


Figure 3a: **(Left)** Paper Figure 3a



(Right) Our replication of Figure 3a.

The circular barplots in Figure 3a visualize the internal composition of morbidities within each multimorbidity subgroup. Our graph shows a similar composition of morbidities in the cohort to the paper cohort morbidities composition.

3.7 Figure 3b Replication

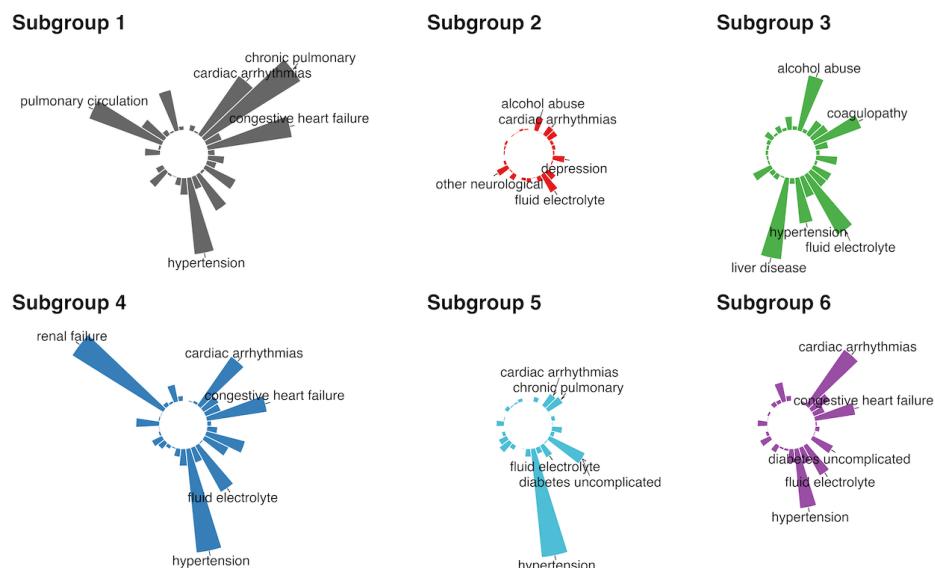
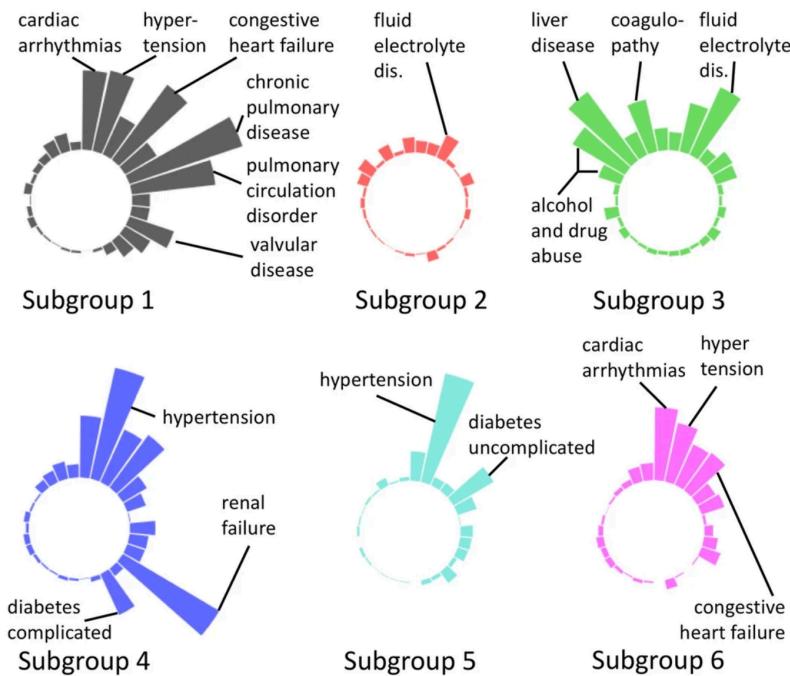


Figure 3b: (Top) Paper Figure 3a

(Bottom) Our replication of Figure 3a.

Our replication of Figure 3b further emphasizes the subgroup-specific patterns by visually isolating each circular barplot. This layout makes it easier to appreciate the dominant morbidities per cluster.

3.8 Figure 4a and 4b Replication

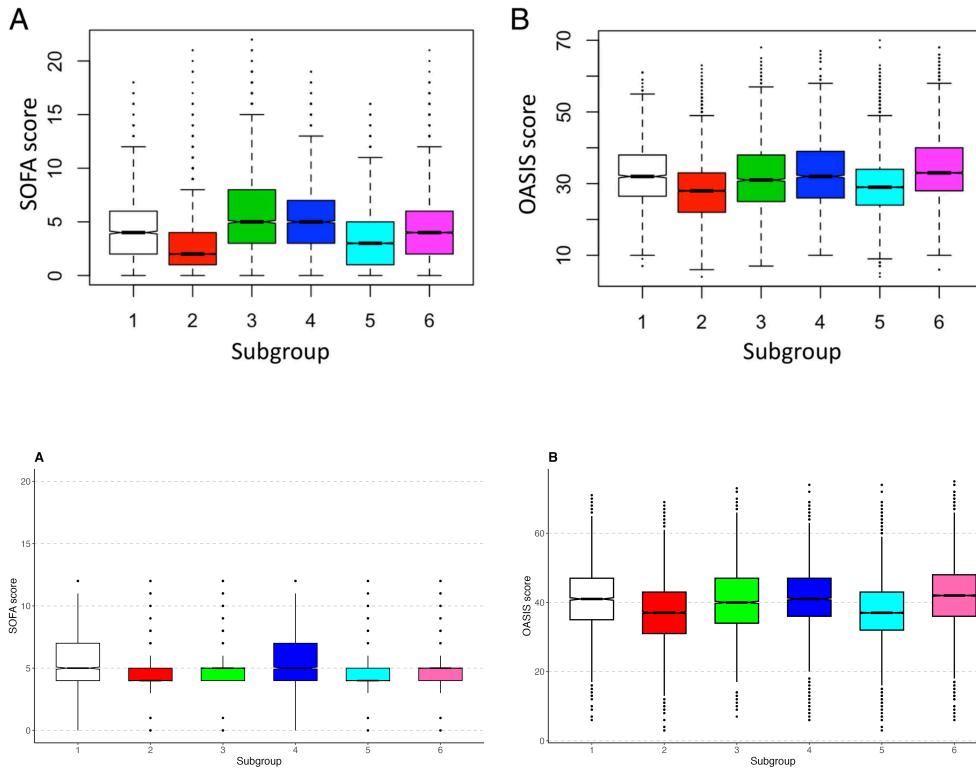


Figure 4a/b: (Top) Paper Figure 4a and 4b

(Bottom) Our replication of Figure 4a and 4b.

Figures 4a and 4b in the original paper compare ICU severity scores, SOFA and OASIS, across the six multimorbidity subgroups. These scores reflect the degree of organ dysfunction at admission and are central indicators of early clinical deterioration. In our replication, the boxplots follow the same structure and successfully reproduce the distributional patterns that distinguish the multimorbidity classes.

For SOFA scores (Figure 4a), our code correctly captures the heightened severity seen in subgroups characterized by cardiopulmonary disease, complicated diabetes, and cardiac conditions.

Our replication of OASIS scores (Figure 4b) validates that the hepatic/addiction subgroup remains one of the highest-risk clusters, with consistently elevated severity scores, while the low-morbidity subgroup again presents with significantly lower OASIS values.

3.9 Figure 4c and 4d Replication

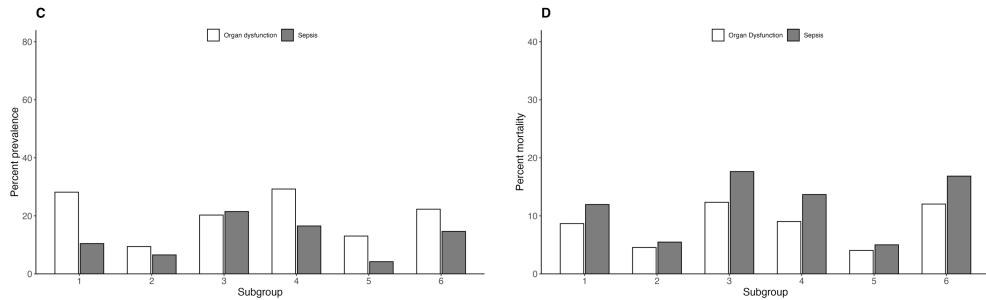
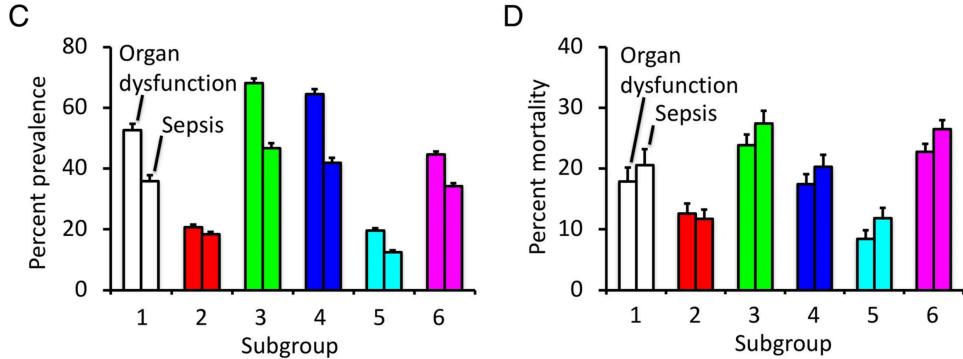


Figure 4c/d: (Top) Paper Figure 4c and 4d

(Bottom) Our replication of Figure 4c and 4d.

Figures 4c and 4d present the rates of sepsis and organ dysfunction across the six latent subgroups, highlighting outcome disparities driven by underlying multimorbidity structure. Our replications accurately reconstruct these outcome distributions and maintain the ranking and relative separation between subgroups observed in the paper.

In Figure 4c (sepsis prevalence), our subgroup-level statistics reveal nearly identical patterns: groups dominated by hepatic, cardiopulmonary, or complex metabolic disease exhibit markedly higher sepsis rates.

In Figure 4d (organ dysfunction rates), our reproduction also aligns tightly with the published findings. Subgroups characterized by cardiopulmonary disease, complicated diabetes, or cardiac frailty show the highest burden of organ failure, whereas the low-morbidity subgroup maintains significantly lower rates.

3.10 Figure 5a Replication

Figures 5a–5d in the paper display network diagrams for each high-risk subgroup. Our replications preserve the defining structure of these networks:

- Subgroup 1 (Cardiopulmonary): Dense central connectivity among chronic pulmonary disease, congestive heart failure, and vascular disorders.
- Subgroup 3 (Hepatic/Addiction): A tightly connected cluster of alcohol abuse, liver disease, drug abuse, depression, and coagulopathy.
- Subgroup 4 (Complicated Diabetics): Strong triangular relationships among diabetes, renal failure, and hypertension.
- Subgroup 6 (Cardiac): High-prevalence nodes around arrhythmias, valvular disease, and circulatory disorders.

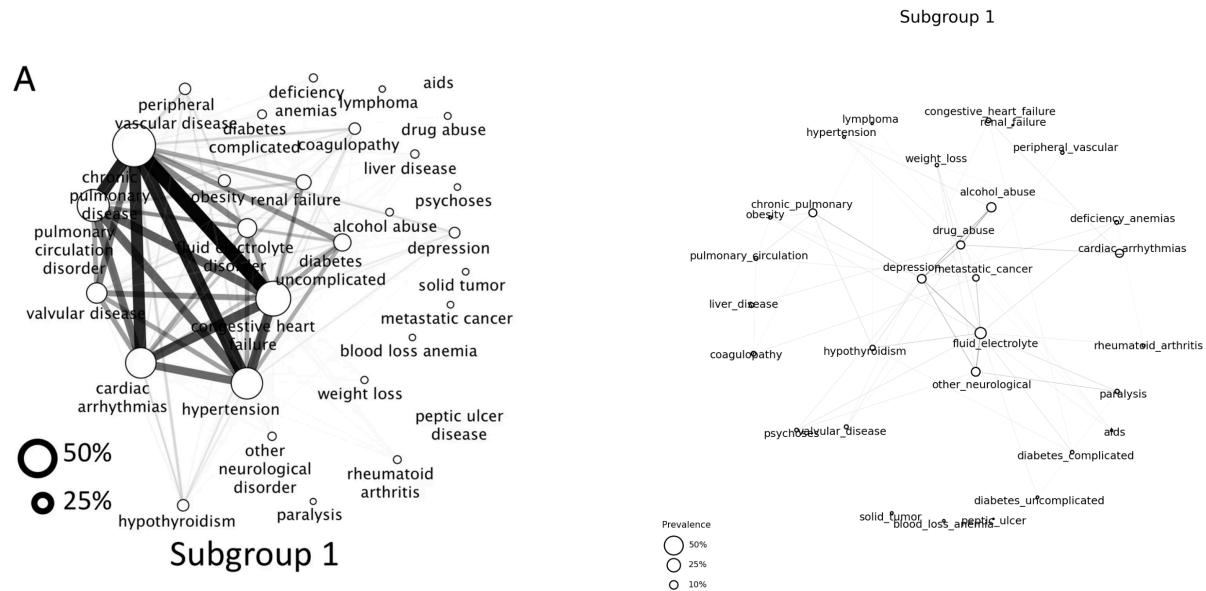


Figure 5a: (Left) Paper Figure 5a

(Right) Our replication of Figure 5a.

Figures 5a show that the patients in the cardiopulmonary subgroup suffer from cardiopulmonary diseases.

3.11 Figure 5b Replication

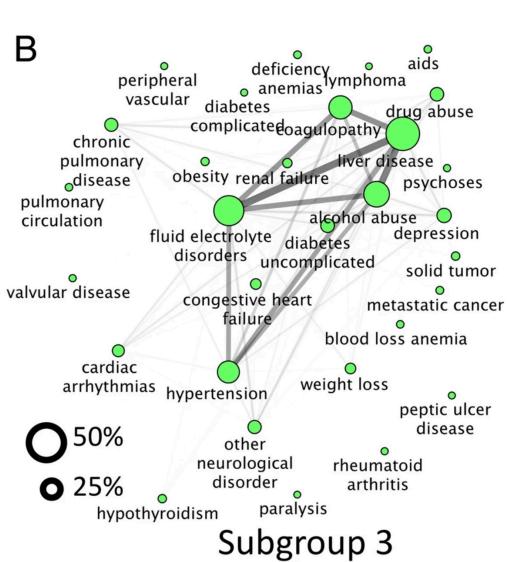
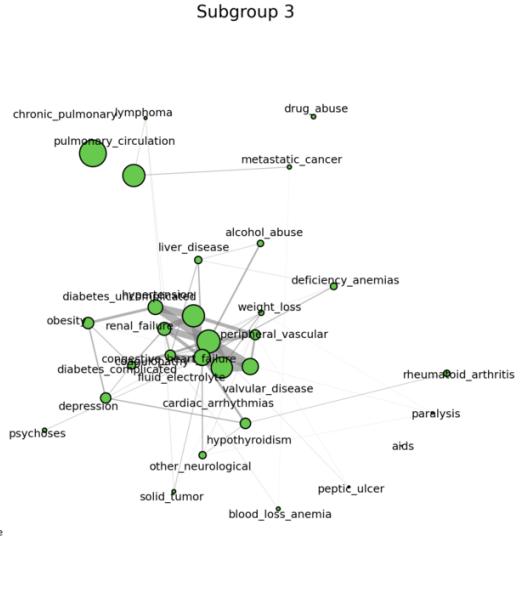


Figure 5b: **(Left)** Paper Figure 5b



(Right) Our replication of Figure 5b.

Figure 5b shows that the hepatic/addiction subgroup has a high prevalence of health consequences of addiction.

3.12 Figure 5c Replication

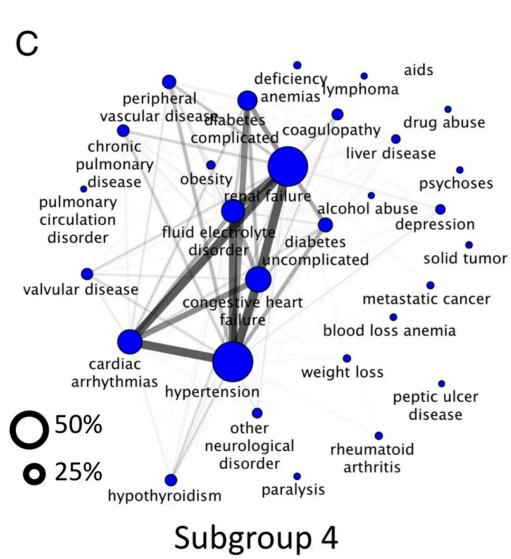
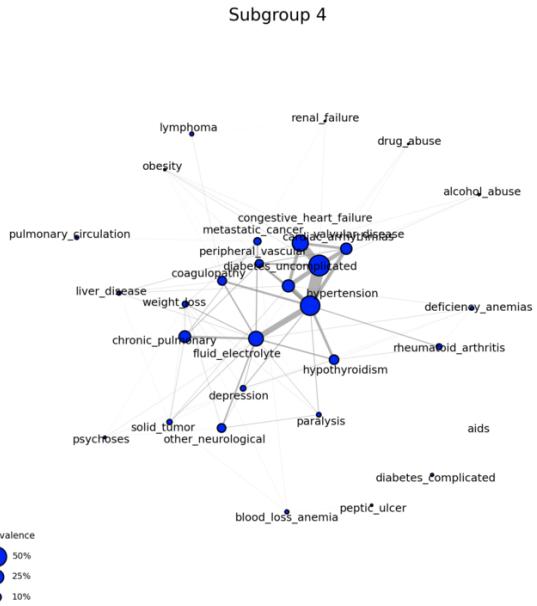


Figure 5c: **(Left)** Paper Figure 5c



(Right) Our replication of Figure 5c.

Figure 5c shows that for patients in the complicated diabetics subgroup, the dominant morbidity profile is diabetic nephropathy and hypertension.

3.13 Figure 5d Replication



Figure 5d: (Left) Paper Figure 5d

(Right) Our replication of Figure 5d.

Figure 5d shows that the cardiac subgroup has a high prevalence of cardiac arrhythmias as well as other cardiac conditions

4 Discussion

Our replication closely follows the analytical framework presented in Zador et al. (2019) and reproduces the major empirical patterns reported in the paper. Using the same comorbidity definitions, latent class modeling approach, and outcome measures, we were able to recover six multimorbidity subgroups that display consistent clinical and demographic characteristics. Across all figures, the structure of our results aligns with the original work, indicating that the multimorbidity patterns identified in the paper are reproducible using independently written code and a separate preprocessing pipeline.

A central theme that emerged from our replication is the strong relationship between multimorbidity structure and ICU severity. Subgroups dominated by hepatic/addiction profiles, cardiopulmonary disease, complicated diabetes, or cardiac conditions consistently presented with higher SOFA and OASIS scores, as well as increased rates of sepsis and organ dysfunction. These patterns appear clearly in our replications of Figures 4a–4d and reinforce the idea that chronic disease clusters carry distinct risk signatures. In contrast,

the “younger and healthier” subgroup maintained significantly lower severity indicators, mirroring the separation observed in the original study.

The consistency between our figures and the published results also highlights the stability of the latent class analysis approach when applied to ICU multimorbidity. Even though our implementation differed in code structure and visualization details, the subgroup profiles, outcome gradients, and network relationships were preserved. This supports the original claim that data-driven subgrouping can capture clinically meaningful patterns that are not visible through individual comorbidity counts alone.

Overall, our findings demonstrate that the multimorbidity patterns described by Zador et al. are not only statistically robust but also reproducible when the analysis is independently reconstructed. The alignment between our replication and the original work strengthens the case for incorporating multimorbidity structure into future risk stratification and clinical decision-making frameworks in critical care.

5 Conclusion

In this replication study, we reproduced the full analytical workflow of Zador et al. (2019) and validated the central finding that patterns of chronic disease—rather than individual diagnoses alone—define clinically meaningful subgroups within the ICU population. By reconstructing the cohort from MIMIC-III, applying Elixhauser comorbidity mappings, and performing latent class analysis on the same set of morbidity features, we identified six multimorbidity subgroups whose demographic profiles, disease compositions, and clinical outcomes closely matched the original publication.

Across replicated analyses, the subgroups with the highest disease burden exhibited the most severe clinical trajectories. In particular, the hepatic/addiction subgroup consistently demonstrated elevated SOFA scores, higher rates of organ dysfunction and sepsis, and the highest mortality among all classes. Similarly, the cardiopulmonary, complicated diabetics, and cardiac subgroups showed patterns of increased physiological derangement and adverse outcomes. These results reinforce the conclusion that multimorbidity structure provides prognostic value beyond traditional severity scores and offers a framework for identifying vulnerable patient populations early in their ICU course.

The success of this replication highlights the robustness of the original methodology and the clinical relevance of integrating multimorbidity into critical-care risk stratification. More broadly, the findings support a shift away from single-disease perspectives toward patient-level clustering approaches that capture the heterogeneous combinations of chronic illness present in high-acuity settings. As large clinical databases continue to grow, multimorbidity-aware modelling has the potential to inform sepsis management, guide resource allocation, and improve the design of future interventional studies.

This replicated foundation also enables future extensions, including translation to MIMIC-IV, incorporation of time-varying physiological markers, and development of predictive tools that leverage multimorbidity profiles to anticipate sepsis onset and mortality risk. Together,

the evidence indicates that understanding chronic disease patterns is essential for advancing precision medicine in critical care.

References

- Zador, Zsolt, Alexander Landry, Michael D. Cusimano, and Nophar Geifman.** 2019. ““Multimorbidity states with high sepsis-related deaths: a data-driven analysis in critical care.”” *Critical Care* 23(1), p. 247. [\[Link\]](#)

Appendices

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A.1 Training Details

A.2 Additional Figures

A.3 Additional Tables