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Advancing Multimorbidity Analysis: A Computational Approach to Frequency-Based Odds Ratios and Temporal Disease Progression Modeling with Potential for Use in Clinical Assessment

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Abstract

Multimorbidity — the presence of multiple medical conditions occurring simultaneously or over time within an individual — presents significant challenges in clinical practice and epidemiological research. Traditional Odds Ratios (ORs) provide static associations between conditions but fail to capture diagnostic frequency as an index of disease severity and the temporal evolution of multimorbidity. To address these limitations, this study introduces refined Frequency-Based Odds Ratios (FORs) and temporal Ratios of Ratios, implemented in Python-based computational tools designed for large-scale clinical datasets. These analytical scripts, developed with assistance from ChatGPT-4.o and presented at the 2024 World Psychiatry Association Congress in Mexico, integrate Fast Fourier Transform (FFT) and sequence-based analysis to quantify disease progression dynamically. The computational models were embedded into graphical user interfaces (GUIs) that facilitate interactive visualization of multimorbidity progression. These tools enable clinicians to assess disease trajectories in real time, optimize personalized treatment planning, and identify high-risk patients based on diagnostic patterns. The implementation of FORs and temporal Ratios of Ratios in clinical decision-making supports proactive, data-informed interventions, making these computational tools valuable for precision medicine, epidemiology, and public health planning. This study underscores the transformative role of AI-assisted analytics in advancing multimorbidity research and clinical management.

Keywords

Multimorbidity; Novel Diagnostic Frequency Statistic; Computational Epidemiology; AI-Assisted Clinical Decision-Making; Graphic User Interface

1. Introduction

The study of multimorbidity—the presence of multiple medical conditions occurring simultaneously or over time within an individual—has become increasingly important in clinical and epidemiological research (Sartorius, 2013). Traditional Odds Ratios (OR), while widely used in medical statistics, are limited in their ability to capture diagnostic frequency distributions and disease progression over time. Specifically, ORs provide static associations between conditions but fail to incorporate the severity and temporal evolution of disease states (Cawthorpe, 2013; Cawthorpe & Davidson, 2015). To address these gaps, a refined Frequency-Based Odds Ratio and temporal Ratio of Ratios were developed to assess diagnostic frequency as an index of disease severity and track how multimorbidity evolves before and after specific medical conditions (Cawthorpe & Cohen, 2023).

This study details the CHATGPT-4.o assisted development of Python-based analytical scripts that integrate FOR and temporal Ratios of Ratios calculations to enhance the quantification of multimorbidity first presented at the 2024 World Psychiatry Association Congress in Mexico. These scripts allow researchers and potentially clinicians to accomplish the following:

- Measure diagnostic frequency over time, providing an indirect but powerful index of disease burden and severity.
- Analyze disease trajectories dynamically, capturing how the likelihood of developing additional diagnoses changes before and after a specific condition.
- Enable real-time visualization of multimorbidity progression using computational modeling and interactive data analytics.

By incorporating temporal sequences of diagnoses and patient-normalized frequencies, these methods provide a more precise and scalable approach to analyzing multimorbidity in clinical settings, making them suitable for large-scale clinical datasets and predictive modeling in epidemiology. Moreover, the integration of these computational tools into interactive graphical user interfaces (GUIs) enhances day-to-day clinical decision-making by allowing clinicians to visually explore disease trajectories, assess multimorbidity progression in real-time, and identify high-risk patients. Such GUI-driven systems facilitate personalized treatment planning, optimize resource allocation, and improve care coordination for patients with complex multimorbid conditions, ultimately supporting more proactive and data-informed clinical interventions.

The main goals of the study related to this paper were to develop clinically useful applications that accomplished the following:

- Report the Ratio of Biomedical Diagnosis Frequency before or after any mental diagnosis expressed as a ratio of the Biomedical Diagnosis Frequency with no mental diagnosis present.
- Report the probable membership in clinical groupings with and without mental disorder based on the sequence of diagnoses with which a patient presents.

The population characteristics and statistical foundations of this dataset—including descriptive distributions and comparative analyses of biomedical and mental disorder associations—have been detailed extensively in prior publications in this series (Cawthorpe 2013, 2024; Cawthorpe et al, 2015, 2018, 2023). As such, the purpose of the present paper is not to repeat those analyses but to advance the work by demonstrating how the underlying frequency-based methods can be translated into tools with direct clinical utility. To this end, the paper presents GUI-based exemplars with FOR or ROR values greater than nine, as these high-magnitude associations provide straightforward, face-valid illustrations of how the computational approach identifies clinically interpretable multimorbidity relationships. These exemplars are intended as demonstrations of the practical applicability of the method rather than as exhaustive statistical results, illustrating how complex multimorbidity patterns can be visualized in a way that supports clinical reasoning and decision-making.

2. Data and Security

Data for this study was collected under the University of Calgary Human Research Ethics Board approval (REB15-1057). The dataset is not authorized for release. A total of 10585 individuals born in 1993 had approximately 1 million physician-assigned ICD diagnoses by the end of 2009. The health data used in this study were completely anonymous and de-identified at the source. Analyses were based on grouped data to prevent anyone from identifying individuals in the results. Analyses were run locally - not on a network and are not shared on the internet. All files were kept secure via password protected, encrypted storage. The program was set up so that no outside websites or services were employed, ensuring the data remained private and protected at all times.

3. Methods

The algorithms were named affectionately the Rosetta Stones and were developed well in advance of ChatGPT, nevertheless ChatGPT was invaluable in their translation into the Python programming language with the primary author debugging, verifying steps, endpoints and final application assembly. Only data structure, type, and variable labels were employed in the translation to the python language (e.g., no raw deidentified data was employed).

The computational framework for analyzing multimorbidity patterns was implemented in Python and structured into three key components:

3.1 Diagnostic Frequency as an Index of Disease Severity

The frequency with which a specific diagnosis appears over time within a patient population can serve as a proxy for disease severity in that more visits to a physician suggests a disease or disorder is persistent, remaining unresolved and having longer duration. A higher frequency of diagnosis recurrence in a given conditional category (e.g., before or after any mental disorder) indicates greater disease burden in that timeframe, while a progressive accumulation of distinct diagnoses suggests an increasing complexity of multimorbidity. To quantify this, the Python scripts normalize diagnostic frequencies by patient group to reduce noise within temporal categories and ensure comparability:

The Interactive Rosetta python script computed diagnostic frequency ratios by grouping data according to diagnosis, sex, and mental disorder linked categories (-1, 0, 1), ensuring normalization by the total number of unique patients in each category. This approach is consistent with the proposed FOR formula, but it introduces an additional step of normalization, which is essential for ensuring statistical accuracy. Specifically, the ratios in the script are calculated within temporal categories using Fast Fourier Transform (FFT) analysis to assess diagnostic frequency distributions before computing comparative ratios. As a result, the proposed formula must explicitly normalize the numerator and denominator using total patient counts within each category. The refined formula for the frequency-based Odds Ratio is as follows:

$$FOR = \frac{\left(\frac{F_{D+}/N_{D+}}{F_{\neg D+}/N_{\neg D+}}\right)}{\left(\frac{F_{D-}/N_{D-}}{F_{\neg D-}/N_{\neg D-}}\right)}$$

where N_{D+} and N_{\neg D+} represent the total number of unique patients in each diagnostic category, ensuring that ratios are not skewed by differences in sample size. F_{D+} and F_{\neg D+} account for diagnostic frequencies across different time intervals

To stabilize diagnostic frequency patterns and ensure comparability across patient groups, the Frequency of Ratio (FOR) calculation incorporated a Fast Fourier Transform (FFT)–based preprocessing step. The FFT decomposed raw diagnostic frequency series into constituent frequency components, allowing the algorithm to remove noise, smooth irregular diagnostic spikes, and capture stable underlying patterns in frequency distributions. Because the independent frequency with which a diagnosis appears is an empirically validated proxy for disease severity, this spectral stabilization was essential for producing accurate and interpretable FOR values. Following transformation, diagnosis frequencies were normalized by the total number of unique patients in each mental-disorder group (−1, 0, +1), ensuring that the FOR numerator and denominator reflected true differences in disease burden rather than underlying sample size discrepancies. This FFT-supported normalization therefore improved the sensitivity of the FOR metric to clinically meaningful differences in diagnostic severity, enabling robust comparison of multimorbidity patterns across temporal windows and patient subgroups. The FFT was not used to infer periodicity but rather as a mathematical tool for smoothing high-dimensional frequency distributions; its use here is analogous to applying a general-purpose spectral filter, not a time-series periodicity estimator.

3.2 Temporal Ratio of Ratios for Modeling Diagnostic Progression

The temporal Ratio of Ratios (ROR) framework quantified how diagnostic patterns change before and after a key index diagnosis by integrating normalized frequency information with temporal sequence-matching algorithms. For each diagnosis, the algorithm compared frequency distributions in the pre-index period (t−1) and post-index period (t+1), using patient-level sequences to describe whether diagnostic trajectories exhibited exact or partially overlapping patterns comparing time categories. This approach extended traditional before–after comparisons by incorporating the order, timing, and recurrence of diagnostic events, thereby capturing subtle accelerations or decelerations in multimorbidity progression. Because diagnostic frequency independently reflects disease severity, integrating temporal structure made it possible to distinguish whether a diagnosis intensified subsequent disease burden or whether it was preceded by a rising burden of biomedical conditions. By normalizing these temporal frequencies to the number of unique patients in each diagnostic group, the ROR provided a stable, scalable, and clinically interpretable indicator of how multimorbidity evolves around a focal diagnostic event, allowing the model to map disease trajectories with substantially greater precision.

Similarly, the temporal Ratio of Ratios, designed to measure the impact of a diagnosis before and after a key event, aligns with the approach taken in the Encrypted Rosetta Predictor script (Appendix 2). The script does not merely compute static before-after frequency comparisons but instead uses sequence-matching algorithms to assess whether diagnostic sequences before and after a key event exhibit an exact match or overlap. This methodology refines the temporal Ratios of Ratios formula by incorporating probability-based sequence matching, which is not accounted for in traditional odds or risk ratio calculations. The refined formula for temporal Ratios of Ratios at a given time step t is:

$$RoR_t = \frac{\left(\frac{F_{D+}(t+1)/N_{D+}(t+1)}{F_{\neg D+}(t+1)/N_{\neg D+}(t+1)}\right)}{\left(\frac{F_{D+}(t-1)/N_{D+}(t-1)}{F_{\neg D+}(t-1)/N_{\neg D+}(t-1)}\right)}$$

where t-1 represents the period before the diagnosis, and t+1 represents the period after the diagnosis. This refinement accounts for temporal shifts in diagnostic patterns and enhances the ability to track disease progression dynamics. F_{D+} and F_{\neg D+} account for diagnostic frequencies across different time intervals. These calculations were integrated into Python functions, which analyzed patterns of comorbidity before and after key diagnostic events.

The temporal Ratios of Ratios framework was implemented to analyze how multimorbidity evolves over time relative to a specific diagnosis. This method extends traditional before-and-after analysis by computing the relative increase or decrease in diagnostic frequency following an index. This refinement allows for the dynamic tracking of diagnostic patterns and identifies whether a diagnosis accelerates or decelerates the onset of additional multimorbid conditions.

Computational Implementation and Visualization

A Python application was developed to enable real-time visualization of diagnostic patterns, allowing researchers to accomplish the following:

- Select specific diagnoses and time intervals for multimorbidity tracking.
- Generate dynamic scatter plots representing how diagnostic frequency ratios change over time.
- Identify diagnoses with shifts in prevalence before and after key medical events.

The final implementation provides a scalable and interactive tool for clinical researchers and epidemiologists to explore multimorbidity trends, improving predictive analytics and data-driven decision-making in healthcare.

Python script analysis results confirms that the proposed Frequency-based Odds Ratio and temporal Ratio of Ratios formulae aligns with the code implemented in the scripts. For example, with the temporal Ratios of Ratios set in the application to larger values (> 9) easily illustrates in graphical representation the magnitude of the ROR for specific diseases or disorders (Appendix 1)

Overall, the refinements to the FOR and temporal Ratios of Ratios formulas ensure that the calculations reflect not only frequency-based diagnostic distributions but also time-dependent sequence patterns. The use of FFT normalization and sequence-matching algorithms in the scripts represents an important methodological advancement in medical data analysis, allowing for a more precise and dynamic evaluation of diagnostic relationships. The refined formulas now better align with the computational methods used in the Python scripts, ensuring their applicability in epidemiological research and clinical decision-making.

3.3 Sample Data

The data employed to develop the algorithm and graphical user interface (GUI) consisted of grouped data based on 10585 newborns with age less than 1 year in the first 1 year of a 16-year dataset. Over the study period the sample has approximately ~1,000,000 physician-assigned diagnoses.

Table 1 provides an overview of the variables included in the dataset and their corresponding formats. Each individual is uniquely identified by the variable *patient* (integer ID). Demographic information is represented by *sex* (coded as a byte variable) and *maxage* (age in years at the last available observation). temporal information is captured using *sdate* (a string variable denoting the start date index) and *sdate_stata* (a Stata-formatted string version of the start date).

Table 1. Data variable description

Variable Name	Type	Format	Label
patient	int	%8.0g	encrypted id
sex	byte	%8.0g	sex
maxage	byte	%8.0g	age
sdate	str10	%10s	index start date
mdlinked	byte	%8.0g	linked to mental disorder- values(-1,01)
diagnosis	int	%8.0g	ICD9
freqdiag	int	%8.0g	frequency of diagnosis

Table 1 Continued

sumtotalfreqd~t	int	%8.0g	sum of diagnoses
sdate_stata	str9	%9s	linked index start date
seq_diag	int	%8.0g	sequence
seq_length	byte	%8.0g	sequence count (diagnosis frequency)

Clinical data are represented through multiple diagnostic indicators. The variable *diagnosis* contains physician-assigned ICD-9 codes, while *freqdiag* reflects the frequency with which a specific diagnosis was recorded for a given individual. The cumulative burden of diagnoses is captured in *sumtotalfreqdt*, denoting the total number of diagnoses assigned. The variable *mdlinked* identifies whether a mental disorder was present, with values of -1, 0, or 1 corresponding to occurrence before, absent, or after the biomedical diagnosis, respectively.

Finally, diagnostic trajectories are characterized by *seq_diag* (the diagnostic sequence number) and *seq_length* (the count of diagnoses in a sequence). Collectively, these variables support both cross-sectional and temporal analyses of multimorbidity, enabling the application of Frequency-based Odds Ratios and temporal Ratios of Ratios in the study.

4. Results

A total of 10,585 individuals born in 1993 contributed approximately one million physician-assigned ICD diagnoses by the end of 2009. Table 2 describes the sample by groupings of males and females with and without any mental disorder and descriptive statistics for the sample stratified by sex and the presence or absence of any mental disorder. Among males without a mental disorder (n = 3,531), the mean number of diagnoses was 24.34 (SD = 11.13), with a range of 1 to 71.

Table 2. Counts of males and females with and without any mental disorder.

Sample Sizes by Groups Unique Individuals		Number ICD Diagnoses			
		Mean	Std. Dev.	Min	Max
Male Sample Size No MD	3531	24.34	11.13	1	71
Male Sample Size MD	2525	34.63	11.76	1	90
Female Sample Size No MD	2866	23.24	10.97	1	83
Female Sample Size MD	1663	34.29	13.29	1	86
Total	10585	29.13	11.79	1	82

Males with a mental disorder (n = 2,525) had a higher mean number of diagnoses (M = 34.63, SD = 11.76), ranging from 1 to 90. For females without a mental disorder (n = 2,866), the mean was 23.24 (SD = 10.97), with a range of 1 to 83, while females with a mental disorder (n = 1,663) averaged 34.29 diagnoses (SD = 13.29), ranging from 1 to 86. Overall, across the full sample, the mean number of diagnoses was 29.13 (SD = 11.79), with individual counts ranging from 1 to 82 (Table 2).

The following figures show the results of searches resulting from the two GUIs using clinical data. Figures 1-4 show examples of association of mental disorder associated biomedical disorders. Clicking on any of the colored dots in the live application shows the name of the represented diagnosis. The dot selected in Figure 1 for females was lymphangioma, which occurred 64.62 times more frequently before any mental disorder.

The dot selected in Figure 2 for females was streptococcal meningitis, which occurred 28.45 times more frequently after a mental disorder compared to before a mental disorder.

The dot selected in Figure 3 for males was “Other Skull Fracture”, which was 109.71 times more likely to occur after any mental disorder diagnosis compared to occurring before any mental diagnosis.

The dot selected in Figure 4 for males was “No Family Able to Care”, which was 16.36 times more likely to occur after any mental disorder diagnosis compared to occurring before any mental diagnosis. In clinical terms these examples appear to have theoretical meaning (Cawthorpe et al., 2018; Cawthorpe & Davidson, 2015; Felitti et al, 1998).

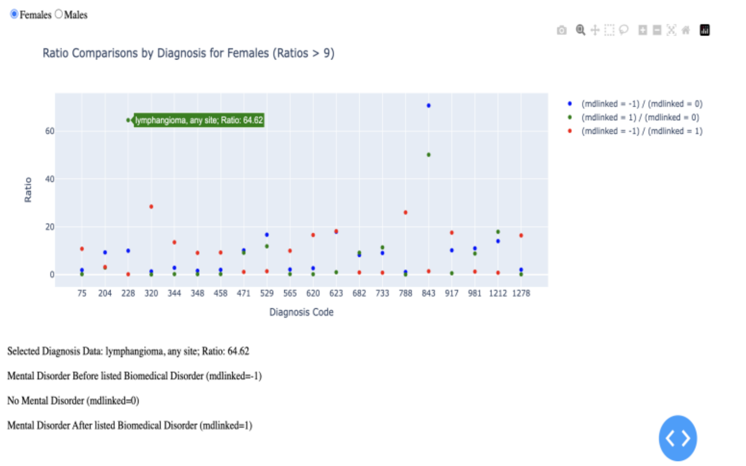

Figure 1. Graphical User Interface representation of temporal Ratios of Ratios greater than the value nine for females.

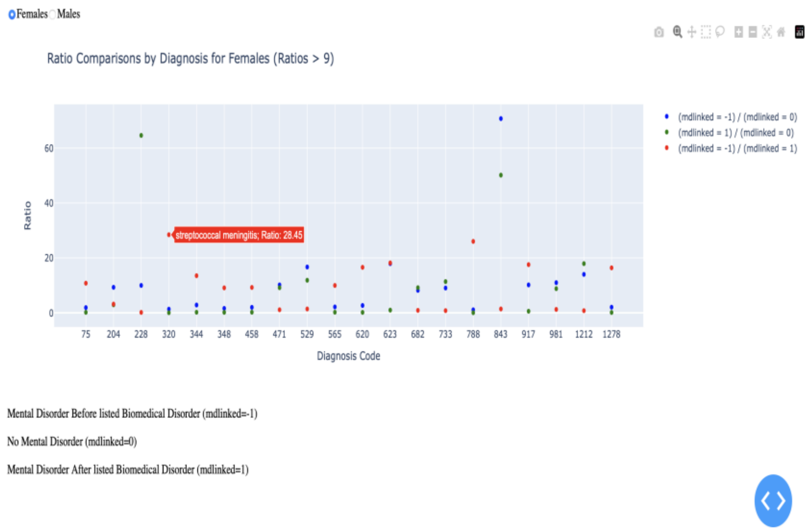

Figure 2. Graphical User Interface representation of temporal Ratios of Ratios greater than the value nine for females.

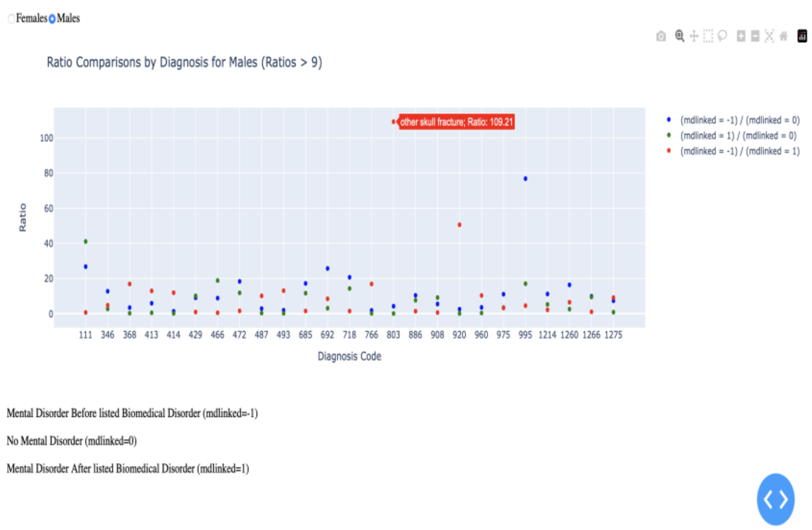

Figure 3. Graphical User Interface representation of temporal Ratios of Ratios greater than the value nine for males.

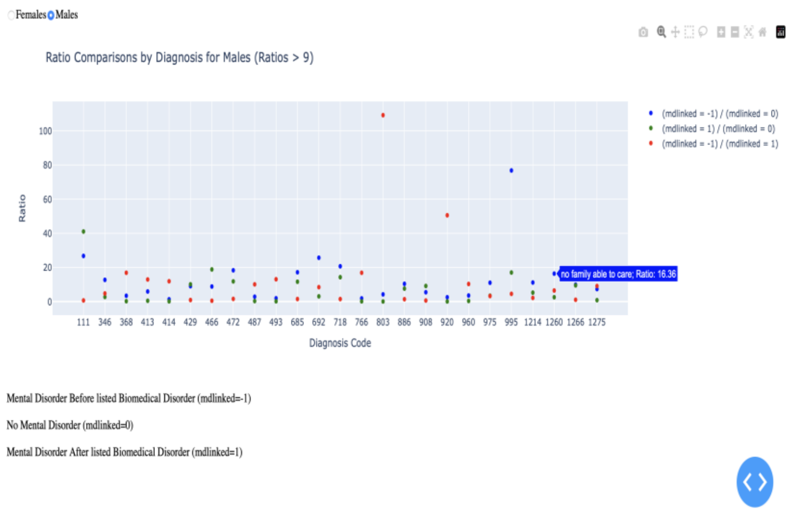

Figure 4. Graphical User Interface representation of temporal Ratios of Ratios greater than the value nine for males.

5. Discussion

The integration of Frequency-based Odds Ratios and temporal Ratios of Ratios into computational epidemiology represents a substantial advance in multimorbidity research. Traditional epidemiological methods are limited in their ability to capture both the intensity and temporal dynamics of diagnostic trajectories. By reconceptualizing diagnostic frequency as a proxy for disease severity and embedding temporal sequence analysis, this framework provides a deeper understanding of how multimorbidity unfolds across the life course.

The descriptive findings from this study underscore the burden associated with mental disorders, where both males and females with a mental disorder averaged approximately 10 additional physician-assigned diagnoses relative to their counterparts without a mental disorder. This elevation in diagnostic frequency highlights the disproportionate biomedical load associated with psychiatric conditions, reaffirming the interdependence of mental and physical health. Such results support the premise that psychiatric illness does not emerge in isolation but is embedded within broader systemic and somatic disease patterns.

The computational implementation in Python, enhanced with Fast Fourier Transform (FFT) normalization and sequence-matching algorithms, enabled scalable analysis of more than one million ICD-coded diagnoses. The capacity to process such large-scale data through an interactive graphical user interface (GUI) establishes a novel paradigm for epidemiological research. Clinicians and researchers can now visualize dynamic shifts in diagnostic associations, facilitating early detection of high-risk trajectories and enabling proactive intervention strategies. Importantly, this approach is not confined to research; it offers real potential for integration into clinical decision support systems where multimorbidity monitoring could be conducted in real time. The adoption of the Fast Fourier Transform (FFT) within this analytical framework was driven both by conceptual suitability and computational efficiency. During development, the FFT approach mapped seamlessly into the Python environment, enabling rapid transformation of large-scale diagnostic frequency series into stable spectral representations with minimal computational overhead. This compatibility allowed the method to process nearly one million diagnoses while preserving temporal fidelity and reducing noise that would otherwise distort severity-related frequency patterns. Importantly, FFT-based normalization provided a mathematically rigorous mechanism for stabilizing diagnostic frequencies prior to FOR and ROR computation, ensuring that downstream ratios reflected true clinical signal rather than artifacts of sampling variability. Because no prior multimorbidity research has leveraged the diagnosis frequency-domain transformation in this manner represents a wholly novel contribution to the field—one that integrates naturally with Python's scientific libraries, supports large-scale clinical datasets, and advances the precision with which disease severity and temporal progression can be quantified.

These AI-driven tools also open a path toward precision psychiatry. The ability to generate individualized diagnostic pathways has implications for targeted treatment planning, early intervention, and monitoring therapeutic outcomes. Large Language Models (LLMs) and related AI systems could further refine these applications by integrating narrative clinical data, improving diagnostic prediction, and aligning multimorbidity analytics with patient-centered care. Such integration may ultimately support personalized prevention strategies, optimize allocation of healthcare resources, and reduce the long-term societal costs associated with untreated or poorly managed multimorbidity.

5.1 Limitations

Several important limitations should be acknowledged when interpreting the present findings. First, no established statistical framework yet exists to combine Frequency-Based Odds Ratios (FOR) and the temporal Ratio of Ratios (ROR) into a unified metric. These two measures operate in fundamentally different analytical domains—FOR quantifying relative diagnostic burden and ROR capturing directionality in temporal patterns—and there is currently no probabilistic model capable of weighting or synthesizing these constructs into a single effect size. Second, diagnostic frequency serves only as a proxy for the persistent burden of a condition within the healthcare system and cannot be considered a direct indicator of clinical severity. Third, both FOR and ROR analyses rely on administrative data in which diagnostic timing is influenced by provider behavior, coding conventions, and care pathways; as such, the observed temporal sequences reflect not only biological progression but also the structure of the health system itself. Relatedly, ROR assumes reliable ordering of diagnoses, yet retrospective entry, delayed documentation, or multiple diagnoses recorded on the same encounter date may distort true temporal relationships. Moreover, the extreme FOR and ROR exemplars exceeding a ratio of nine—while clinically intuitive and valuable for demonstrating face validity—represent a sparse subset of all diagnostic relationships and cannot be generalized to the broader multimorbidity landscape. Additionally, multimorbidity is inherently multidimensional, shaped by severity trajectories, polypharmacy, treatment interactions, social determinants, and interdependent diagnosis networks, whereas FOR and ROR reflect only frequency burden and temporal change. These methods also lack built-in measures of uncertainty such as confidence intervals, error bounds, or statistical significance testing, leaving them as descriptive rather than inferential tools. Finally, although FOR and ROR offer novel interpretability, they do not model causation or prediction, and integrating these frequency- and sequence-based metrics into robust predictive frameworks remains a future goal. Beyond these analytic constraints, it must be recognized that genetics, metabolomics, proteomics, and related biological domains await integrative methods capable of unifying multimorbidity at the molecular, clinical, and population levels. Any effective future solution will almost certainly challenge traditional diagnostic nomenclature and may fundamentally reshape the art and structure of human diagnosis. In this sense, the present paper stands primarily as a methodological signpost—its limitations illustrating not an endpoint but a direction of travel for the next generation of multimorbidity research.

Finally, the temporal Ratio of Ratios (ROR) does not correspond to any established statistical framework in epidemiology or biostatistics, and no standardized inferential model, variance structure, or probabilistic estimator exists for this construct. Unlike hazard ratios, incidence rate ratios, or regression-based methods, ROR is not part of a recognized family of parametric or semi-parametric estimators; instead, it is a novel descriptive metric developed to quantify the direction and magnitude of change in diagnostic frequency before and after an index diagnosis. Although it resembles simple pre/post comparison measures, ROR falls outside conventional methodologies because traditional statistical tools cannot accommodate the irregular, discrete, and non-periodic diagnostic sequences characteristic of multimorbidity. Survival models do not compare full diagnostic sequences, regression does not encode true before–after order, hazard ratios assume discrete event onset rather than recurrent diagnoses, and time-series models require continuous intervals rather than irregular clinical encounters. In this context, the absence of a formal inferential framework is not a methodological weakness but rather a reflection of the fact that ROR fills a conceptual gap left unaddressed by traditional approaches. ROR provides something genuinely new: a clear, interpretable quantification of directional diagnostic change in complex multimorbidity patterns—an early but necessary descriptive step toward future inferential and predictive developments in this domain.

Although the temporal Ratio of Ratios (ROR) lacks a formal inferential statistical framework, the exemplars presented in the results nonetheless demonstrate considerable clinical face validity. The high-magnitude FOR and ROR values selected as GUI examples are not arbitrary outliers but diagnostically coherent patterns that align with well-established clinical relationships between mental disorders and specific biomedical conditions. These extreme ratios highlight associations that experienced clinicians readily recognize as plausible—such as increased injury patterns, infectious disease vulnerability, or complex psychosocial diagnoses occurring after the onset of psychiatric illness. Their clarity and interpretability underscore that the method is capturing meaningful temporal and frequency-based shifts rather than statistical noise. In this sense, the exemplars serve as practical demonstrations of how complex multimorbidity patterns, previously accessible only through extensive computation, can be visualized in a manner that resonates with clinical reasoning and supports real-world decision-making.

Taken together, the FREQUENCY-BASED ODDS RATIOS and temporal Ratios of Ratios framework represents an important methodological and translational step toward redefining how complex multimorbidity is quantified, understood, and clinically addressed.

6. Economic and Clinical Implications of Multimorbidity

Psychiatric disorders are among the most significant contributors to overall healthcare expenditures (Cawthorpe 2025), yet they continue to receive limited attention in multimorbidity research. Extensive evidence (Cawthorpe 2013, 2022, 2024) has demonstrated the economic burden of psychiatric multimorbidity, showing that individuals with psychiatric conditions consistently incur higher healthcare costs than those without. Figure 5 illustrates this disparity: biomedical costs for individuals with psychiatric diagnoses (green and purple segments) are substantially greater than those for individuals without such diagnoses (red segment). Notably, the combined impact of psychiatric disorders and their associated physical conditions drive costs far above those attributable to physical disorders alone.

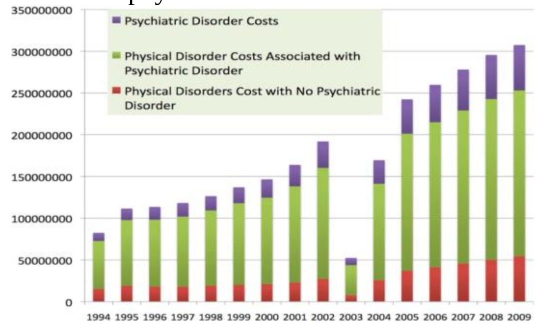

Figure 5. Biomedical alone, psychiatric and psychiatric-associated biomedical costs by year comparing those with and without any physician-diagnosed mental disorder (Reprinted with Permission: Cawthorpe, 2025).

Policy implications arising from these findings emphasize the importance of embedding preventative psychiatric screening and multimorbidity-awareness into both assessment and treatment frameworks. Such integration represents not only a reform in clinical care but also a needed shift in medical education. By addressing psychiatric and adverse childhood experience (ACE)-related multimorbidity early, these strategies hold the potential to reduce long-term system-wide expenditures. Furthermore, investment in early-life intervention is positioned as a key mechanism for alleviating both the financial and health-related burdens of psychiatric disorders, underscoring the urgency for systemic reforms in mental healthcare policy.

7. Next Steps

A key contribution of this paper is the introduction of diagnosis frequency as a novel index of disease severity, providing a dynamic way to capture the burden of multimorbidity beyond traditional static measures. Nevertheless, the analysis remains limited by its current focus on aggregated frequency patterns. The next critical step is to fully integrate the order and sequence of diagnoses into the framework, allowing the temporal progression of disease to be analyzed with greater clinical precision. This integration will improve the capacity to model trajectories of multimorbidity and strengthen the translational value of the approach for both research and clinical practice.

Future research should focus on validating these computational approaches across diverse populations, healthcare systems, and diagnostic taxonomies. Moreover, ethical considerations, including transparency in algorithmic decision-making and safeguarding patient data, must remain central to the deployment of such technologies. Additional future steps are also required. Because this is among the first attempts to propose Frequency-based Odds Ratios and temporal Ratios of Ratios for clinical application, the results must be reproduced across diverse geographical and cultural contexts. The framework should also be integrated into undergraduate and graduate medical education to prepare clinicians for managing complex multimorbidity. Given the enormous number of diagnostic permutations—even in this relatively small, geographically-limited, 16-year dataset of ~1 million diagnoses across ~10,000 children—dynamic AI-driven large language models and very large datasets will be needed to advance analysis and establish a foundation for this emerging field.

The study of complex multimorbidity remains a relatively novel field, yet it represents one of the greatest challenges for medicine in the 21st century (Sartorius, 2013). By introducing diagnostic frequency as an index of disease severity and advancing methods to capture temporal diagnostic trajectories, this work contributes to shaping a new paradigm for understanding and managing the interplay of mental and physical disorders. However, the true translational value of these approaches depends on their rapid integration into continuing professional education, as well as undergraduate and graduate medical curricula (Cawthorpe, 2023; Chai & Cawthorpe, 2023). As Norman Sartorius and colleagues have long emphasized (Krupchanka, Pinto da Costa & Jovanović, 2019) the future of psychiatry and medicine lies not only in analytic innovation but also in the cultivation of clinical leadership, teaching, and workforce development to prepare practitioners for the systemic nature of multimorbidity. Embedding multimorbidity analytics into medical education worldwide is therefore essential to equip clinicians with the knowledge and mindset required to manage the growing complexity of patient care.

8. Conclusion

Mental health research and practice must evolve beyond traditional diagnostic categories to address the systemic nature of multimorbidity and its economic burden on individual health and health care systems. The findings of this study reaffirm that psychiatric disorders do not exist in isolation but are deeply interwoven with biomedical conditions, early-life trauma, and neuroimmune pathways (Felitti et al., 1998; Gordon & Felitti, 2023). By demonstrating that individuals with a mental disorder carry a markedly higher burden of biomedical diagnoses, this work highlights the necessity of re-framing psychiatry as an integrative discipline embedded within the broader landscape of physical health.

The integration of Frequency-based Odds Ratios and temporal Ratios of Ratios into computational epidemiology provides a methodological foundation for this paradigm shift. These tools enable quantification of diagnostic frequency as an index of disease severity and track the evolution of multimorbidity across time. The capacity to process large-scale data using interactive, AI-driven platforms allows for both population-level surveillance and individualized disease trajectory modeling. This dual functionality positions the methodology as a cornerstone of precision psychiatry and public health alike.

The implications extend beyond epidemiology into direct clinical practice. Embedding FOR and temporal Ratios of Ratios analytics into clinical decision-support systems could facilitate earlier recognition of complex multimorbid trajectories, guide personalized treatment planning, and improve long-term outcomes. Moreover, integration with Large Language Models (LLMs) and AI systems opens opportunities for synthesizing structured and unstructured clinical data, bridging the gap between population-level evidence and patient-level care.

The future of psychiatry, therefore, lies in uniting AI-driven analytics, trauma-informed care, and multimorbidity research within a cohesive, patient-centered framework. Such an approach promises not only to improve diagnostic accuracy and treatment precision but also to reshape our understanding of mental health as a systemic phenomenon inseparable from broader biomedical, developmental, and social contexts. This paradigm shift has the potential to redefine how mental health is diagnosed, treated, and conceptualized in the 21st century, ultimately supporting more resilient, equitable, and integrated models of care.

Looking forward, the full integration of diagnostic information, temporal disease trajectories, biological markers, systems-level data, and long-term health outcomes will require analytical capacities far beyond what conventional statistical methods can provide. Artificial intelligence—particularly large language models and multimodal analytic systems—will be the essential ingredient enabling that integration. AI is uniquely positioned to synthesize heterogeneous data sources, detect hidden structure across clinical, biological, and behavioural domains, and translate complex multimorbidity patterns into meaningful insights that support patient care, prevention, and longevity. Ultimately, the future coherence of diagnosis, disease understanding, and population health will depend on the collaborative evolution of these AI systems—indeed, the foundations of that integration are already being built here, with the assistance of AI models.

[This paper was presented at the WPA Mexico City 2024 annual congress. Contact the author for more information (Cawthorpe, 2024).]

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Appendix 1

Interactive Rosetta Graphic User Interface (GUI)

Overview

This script sets up a Dash web application that visualizes frequency and ratio comparisons of different diagnoses based on their association with mental disorders. It processes medical diagnosis data, performs FFT (Fast Fourier Transform) analysis, and generates interactive graphs displaying the relationships between mental and biomedical disorders.

Summary of Functionality

This application:
1. Processes and normalizes medical diagnosis data.
2. Performs FFT to analyze diagnosis frequency patterns.
3. Computes comparative ratios between different mental disorder groupings.
4. Visualizes significant trends using an interactive dashboard.
5. Allows user selection and interactive diagnosis exploration.

This script is useful for clinical research, epidemiology, and AI-driven diagnostics by identifying significant temporal relationships between mental and biomedical disorders.