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Multicomorbidity in Psoriasis Vulgaris: A Retrospective Analysis

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Background: The frequencies of comorbidities in patients with psoriasis have been compared to that in the general population in many studies. Moreover, several studies have investigated the risk factors influencing the number of comorbidities in patients with psoriasis. However, a few studies have examined clusters of patients with psoriasis according to their comorbidities. In this study, we aimed to explore the multicomorbidities of psoriasis vulgaris in terms of risk factors and clusters.

Methods: All diagnoses of 452 patients with psoriasis vulgaris were extracted from electronic medical records of a tertiary hospital. Binary association coefficients were calculated for all pairs of comorbidities. Subsequently, a hierarchical cluster analysis was performed.

Results: Among the patients, 30.5% had no comorbidities, 28.8% had a single comorbidity, and 40.7% had multiple comorbidities. The number of comorbidities was positively associated with age and follow-up duration but not with sex. The most striking cluster of comorbidities was composed of diabetes, hepatosteatosis, hyperlipidemia, hypertension, cancer, and cardiovascular disease.

Conclusion: This cluster could be explained by cardiometabolic multimorbidity. Exploring such clusters may provide a more forward-looking perspective for the management of psoriasis patients.

Keywords: psoriasis vulgaris, comorbidities, cluster analysis, retrospective

Introduction

Historically, psoriasis was thought to be limited to the skin. However, it is now recognized as a systemic, chronic inflammatory disease associated with various comorbidities.[1] The pooled relative risk for comorbidities in patients with psoriasis was found to be 1.2 in a meta-analysis published in 2022.[2] The percentages of psoriatic patients without comorbidities, with only one comorbidity, and with multiple comorbidities were reported to be 32.3%, 24.2%, and 43.5%, respectively, in a study published in 2021 and 31.4%, 20.2%, and 48.4%, respectively, in a study published in 2023.[3,4] Whereas multiple comorbidities have been found to be more common in older patients, sex had no effect on the number of comorbidities.[5]

A few studies have attempted to identify clusters of patients with psoriasis based on their comorbidities. By using latent class analysis, Wu et al defined four distinct classes, namely "relatively healthy", "metabolic syndrome", "hypertension and chronic obstructive pulmonary disease", and "multicomorbidity" classes.[6] Again by using latent class analysis, Chalitsios et al categorized psoriatic patients into five distinct classes.[7] High probabilities were observed for hypertension and type 2 diabetes in class 1; for chronic obstructive pulmonary disease, asthma, coronary artery disease, and depression in class 2; for psoriatic arthritis, rheumatoid arthritis, depression, and hypertension in class 3; and for coronary artery disease, heart failure, atrial fibrillation, hypertension, and type 2 diabetes in class 4. Class 5 comprised relatively healthy patients.

The main aim of this study was to determine the number and clusters of comorbidities and factors influencing this number in patients with psoriasis vulgaris who were diagnosed and followed up in our department. Defining comorbidity

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clusters provides better management of psoriatic patients since if two comorbidities are known to be associated with each other, and if a given patient has one of them, the dermatologist should be watchful of the other comorbidity during the patient's follow-up.

Materials and Methods

Study Design and Patients

Electronic medical records of our hospital were scanned to extract the characteristics of patients who were followed up with a diagnosis of psoriasis vulgaris in our department during the 5-year period ending on March 1, 2024. Because the International Classification of Diseases 10th Revision (ICD-10) was used in these records, the code "L40.0" corresponding to psoriasis vulgaris was used in the scanning. As a result of this scan, 687 patients with psoriasis vulgaris were identified. However, some patients visited our department only once. Therefore, patients who were followed up for less than a year were excluded, leaving 452 patients for evaluation. Informed consent was obtained from each patient. Ethical approval was provided by the Medical Ethics Committee of the Cukurova University Medical School (date: 05.04.2024, number: 143).

All diagnoses of these patients were extracted from records covering the 10-year period ending on March 1, 2024. These diagnoses were established not only by our dermatology department, but also by other departments within our hospital. All diagnoses were reviewed, and the following 14 headings were selected as comorbidities: cancer, cardiovascular disease, chronic pulmonary disease, diabetes, hepatosteatosis, hyperlipidemia, hypertension, inflammatory bowel disease, neurological disease, psoriatic arthritis, psychiatric disorder, thyroid disease, tuberculosis, and viral hepatitis. The comorbidities and their corresponding ICD-10 codes are listed in Table 1.

Statistical Analyses

For the analysis, the age at the last visit was designated as "patient age". Differences between the dates of first and last visits were accepted to be "follow-up duration". The number of comorbidities for each patient was determined. The effect of binary variables, such as sex, on this variable was evaluated using the Mann–Whitney *U*-test. Spearman's rank correlation coefficient was used to detect associations between the number of comorbidities and other numerical variables, namely, patient age and follow-up duration.

Cole's coefficients between pairs of binary variables corresponding to each comorbidity were calculated to find distances for the hierarchical cluster analysis.[8] In Cole's coefficient, higher values indicate stronger associations. Such an association should have a lower value for the hierarchical cluster analysis distances. Therefore, the association

Table 1 ICD-10 Codes Used for Extracting Comorbidities from Medical Records in This Study

Comorbidity	ICD-10 Codes
Cancer	C00–C97, D46
Cardiovascular disease	I20–I25, I26–I28, I47–I49, I50, I70, I71, I73, I80, I82, I83, I87, K64
Chronic pulmonary disease	J42, J43, J44, J45, J84
Diabetes	E10–E14
Hepatosteatosis	K76.0
Hyperlipidemia	E78
Hypertension	I10–I15
Inflammatory bowel disease	K50, K51
Neurologic disease	G20, G30, G35, G40, G43, G46, I60–I69, G47, G70, G71
Psoriatic arthritis	L40.5, M07
Psychiatric disorder	F10, F20, F28, F29, F30–F39, F40–F48, F51, F91, F92
Thyroid disease	E00–E07
Tuberculosis	A15–A19, B90, Z03.0
Viral hepatitis	B15–B19

coefficients were subtracted from 1 to obtain distances. Ward.D linkage method was used for the hierarchical cluster analysis. Analyses were performed using R software.[9]

Results

Of the 452 patients with psoriasis vulgaris, 223 (49.3%) were female and 229 (50.7%) were male. The mean age of the patients was 43.1 (SD ±16.5, range 3.9–81.9, median 44.3, 1st quartile 29.9, and 3rd quartile 55.4) years. The mean follow-up duration was 5.6 (SD ±2.9, range 1.0–10.2, median 5.4, 1st quartile 2.9, and 3rd quartile 8.3) years. The most common comorbidities were psoriatic arthritis in 174 (38.5%) patients, diabetes in 116 (25.7%) patients, and psychiatric disorders in 70 (15.5%) patients. The comorbidities and their frequencies are listed in Table 2.

The number of comorbidities per patient ranged from zero to eight. No comorbidities were observed in 138 (30.5%) patients. The number of comorbidities was one in 130 (28.8%) patients, two in 73 (16.2%) patients, three in 45 (10.0%) patients, four in 27 (6.0%) patients, five in 13 (2.9%) patients, six in 17 (3.8%) patients, seven in 5 (1.1%) patients, and eight in 4 (0.9%) patients (Figure 1). The mean number of comorbidities was 1.6 (SD ±1.8, range 0–8, median 1, 1st quartile 0, and 3rd quartile 2) for females. This figure was 1.7 (SD ±1.8, range 0–8, median 1, 1st quartile 0, and 3rd quartile 2) for males. This difference was not statistically significant ($p > 0.05$). However, there were significant positive correlations between the number of comorbidities and both patient age ($r = 0.36$, $p < 0.001$) and follow-up duration ($r = 0.40$, $p < 0.001$).

When psoriatic arthritis was excluded from the comorbidities, the mean number of comorbidities was 1.1 (SD ±1.6, range 0–8, median 1, 1st quartile 0, and 3rd quartile 1) in patients without psoriatic arthritis. This figure was 1.6 (SD ±1.7, range 0–7, median 1, 1st quartile 0, and 3rd quartile 3) in patients with psoriatic arthritis. This difference was statistically significant ($p < 0.001$).

The heatmap and the dendrogram of the hierarchical cluster analysis are shown in Figure 2. Comorbidities were categorized into three main clusters. The first cluster was composed of tuberculosis, inflammatory bowel disease, psoriatic arthritis, and viral hepatitis. The second cluster had two subclusters. While psychiatric disorder and thyroid disease were gathered together, chronic pulmonary disease and neurological disease did so. The third cluster also had two subclusters. The first subcluster was composed of diabetes and hepatosteatosis. Hyperlipidemia, hypertension, cancer, and cardiovascular disease were collected together to form the second subcluster.

Discussion

For simplification, the number of comorbidities could be categorized into “no comorbidity”, “singular comorbidity”, and “multiple comorbidities”. The last one may also be called to be “multicomorbidity”. In a real-world evidence from 1157

Table 2 Frequencies of Comorbidities Found in 452 Patients with Psoriasis Vulgaris

Comorbidities	*n*	%
Psoriatic arthritis	174	38.5
Diabetes	116	25.7
Psychiatric disorder	70	15.5
Cardiovascular disease	64	14.2
Hypertension	59	13.1
Thyroid disease	53	11.7
Chronic pulmonary disease	37	8.2
Hyperlipidemia	34	7.5
Neurologic disease	33	7.3
Hepatosteatosis	32	7.1
Viral hepatitis	31	6.9
Cancer	26	5.8
Tuberculosis	16	3.5
Inflammatory bowel disease	8	1.8

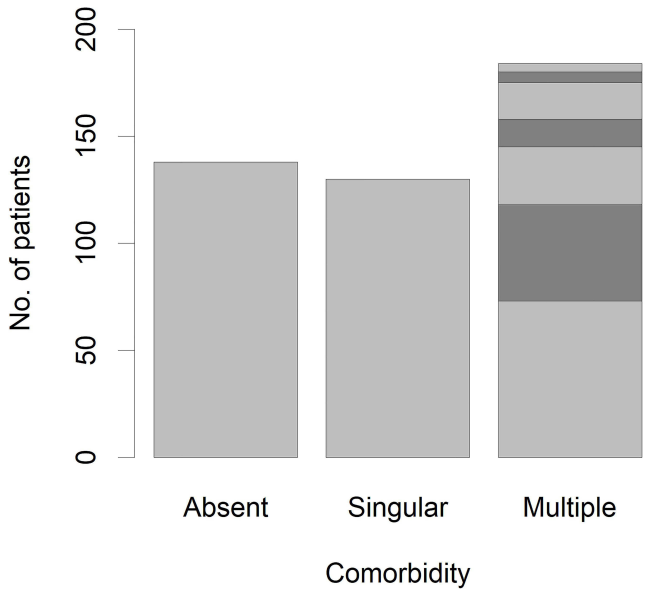

Figure 1 Distribution of the number of comorbidities in 452 patients with psoriasis vulgaris: (The slices from bottom to top of the bar labeled "Multiple" correspond to the number of patients having 2, 3, 4, 5, 6, 7, and 8 comorbidities, respectively).

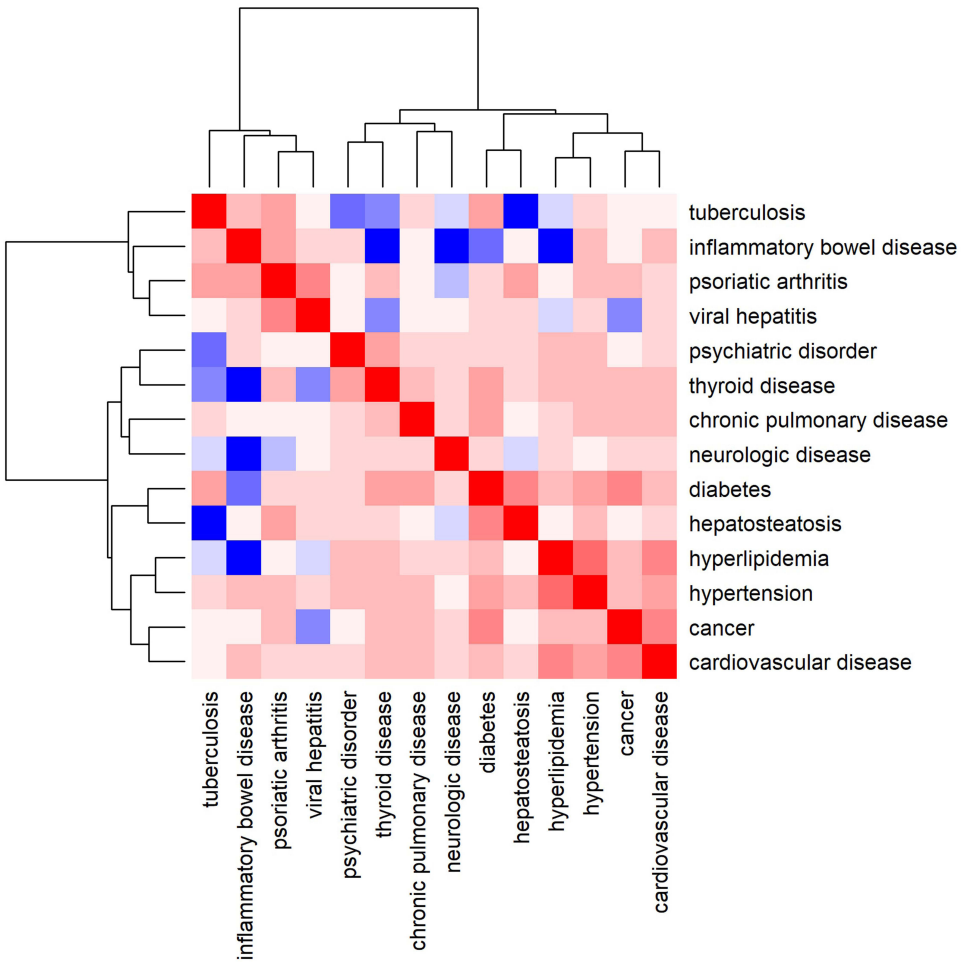

Figure 2 The heatmap and the dendrogram of the hierarchical cluster analysis for comorbidities of psoriasis vulgaris in 452 patients.

psoriatic patients treated with adalimumab, "no comorbidity" was detected in 32.3% of patients, "singular comorbidity" in 24.2%, and "multicomorbidity" in 43.5%.[3] In a matched case-control study determining the initial burden of comorbidities in 28,614 psoriatic patients, these figures were found to be 31.4%, 20.2%, and 48.4%, respectively.[4] Our figures were similar to those of these studies.

As the number of comorbidities increased, a significant increase in the mean age of psoriatic patients was observed.[10,11] When psoriatic patients were categorized into three age groups, multicomorbidity was found to be significantly more common in the older group than in other groups.[5] A difference was usually not observed in studies comparing psoriatic females and males in the number of comorbidities.[5,10–12] We also observed a significant positive correlation between the age of patients and the number of comorbidities, whereas there was no effect of sex on this number. Just as the number of comorbidities was positively associated with the duration of psoriasis in previous studies, we observed a positive correlation between this figure and follow-up duration.[10,11]

In psoriatic patients with arthritis, the most common case was found to be "no comorbidity" in two studies and "multicomorbidity" in one study.[5,10,11] In a study encompassing 20678 psoriatic patients, when comorbidities were considered one by one, many of them were detected more frequently in patients with arthritis than in those without arthritis.[13] Moreover, in the same study, the average Charlson Comorbidity Index score, which is calculated by the sum of weights differing for each comorbidity, was found to be higher in patients with arthritis. Our study also revealed the association between psoriatic arthritis and other comorbidities of psoriasis.

Is it usual for psoriatic patients to have multiple comorbidities? The answer is "yes" according to the present study and those mentioned above. Then, a new question should be asked. Are certain comorbidities associated with others? To answer this question, the classes or clusters of comorbidities should be investigated. One method for such an investigation is latent class analysis. Such an analysis has been performed at least twice for psoriasis.[6,7] In these studies, psoriatic patients were categorized into classes. For example, the probability of hypertension was high in three out of four classes in the first study and in three out of five classes in the second study. Suppose we have detected hypertension in one of our psoriatic patients. Then, by reviewing the classes from a latent class analysis, we can not find a clear answer regarding which other comorbidities have an increased risk. Medical practice can not be easily guided by uncertain suggestions.

Hierarchical cluster analysis is another method for investigating the clusters of comorbidities.[14] Although some of its results are not easily explainable, it always gives a clear answer to the question mentioned above. This case usually facilitates medical practice. Since we used this method, results of our study will likely make easier to manage psoriatic patients.

Comorbidities of psoriasis are important determinants of treatment selection particularly in moderate or severe cases.[15–17] Comorbidities may be linked to psoriasis pathogenetically, as in the concept of psoriatic march, or they may be related to its treatment modalities.[18,19] Whereas some comorbidities such as hypertension have both kinds of relationship with psoriasis, some comorbidities such as tuberculosis and viral hepatitis are only related to treatment modalities such as methotrexate and biological drugs. The latter comorbidities are usually investigated and detected only if these drugs are to be used. This case could explain the gathering of psoriatic arthritis, tuberculosis, and viral hepatitis together in our first cluster, since methotrexate and biological drugs are prescribed to psoriatic patients with arthritis more commonly.

Since it has been stated that mental symptoms are seen in most adults with thyroid dysfunction, the association between psychiatric disorder and thyroid disease in our second cluster is explainable.[20] However, the association between chronic pulmonary and neurological diseases is difficult to explain.

As for our third cluster, if we exclude cancer, this cluster reminds us of cardiometabolic multimorbidity, defined as the co-existence of at least two of three diseases, namely diabetes, coronary heart disease, and stroke.[21] This multimorbidity may also be associated with other diseases such as hypertension, hyperlipidemia, and hepatosteatosis. Clusters suggesting cardiometabolic multimorbidity may also be seen in dendrograms of studies investigating multimorbidity or comorbidity patterns in the general population or in patients with a specific disease, such as HIV.[22,23] Therefore, such clustering is not specific to psoriasis. Exploring cause-effect relationships underlying this clustering may not provide a better understanding the pathogenesis of psoriasis. Instead of such an effort, for example, if a patient has hypertension, he should be closely followed up for cardiovascular disease, hyperlipidemia, hepatosteatosis, and diabetes.

The limitations of the present study are its retrospective nature and the absence of obesity within the list of comorbidities. The reason for this exclusion was that there were only a few patients with a diagnosis of obesity in the electronic medical records. In our country, this diagnosis was not necessary for the prescription of any drug during the time span of the study period. However, a consistent diagnosis should be recorded to prescribe drugs for the treatment of the comorbidities included in the study. Because of this redundancy, physicians may neglect to record "obesity" as a diagnosis. We verified this assumption by the very rare detection of this diagnosis in a sample of records belonging to all patients who were admitted to our hospital. As the information on the diagnosis of obesity was not reliable, we did not include it.

Our findings remind a proverb. "Misfortunes never come singly". According to the present and previous studies, patient age, disease duration, and follow-up duration are positively associated with the number of comorbidities. All of them are simply aspects of time. New ones are added to the comorbidity burden, as time passes. Therefore, physicians managing psoriatic patients should be awake for comorbidities now and tomorrow.

Ethical Approval

Ethical approval was provided by the Medical Ethics Committee of the Cukurova University Medical School (date: 05.04.2024, number: 143). Informed consent was obtained from each patient. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Marson JW, Snyder ML, Lebwohl MG. Newer therapies in psoriasis. *Med Clin North Am*. 2021;105(4):627–641. doi:10.1016/j.mcna.2021.04.004
2. Tang X, Chen L. The risk of organ-based comorbidities in psoriasis: a systematic review and meta-analysis. *An Bras Dermatol*. 2022;97(5):612–623. doi:10.1016/j.abd.2021.10.007
3. Kojanova M, Cetkovska P, Strosova D, et al. Real-world evidence from more than 1000 patients treated with adalimumab for moderate-to-severe psoriasis in the Czech Republic. *Dermatol Ther*. 2021;11(2):543–553. doi:10.1007/s13555-021-00499-8
4. Buja A, Miatton A, Cozzolino C, et al. The prevalent comorbidome at the onset of psoriasis diagnosis. *Dermatol Ther*. 2023;13(9):2093–2105. doi:10.1007/s13555-023-00986-0
5. Alajmi RS, Alamoudi SM, Alabbasi AA, Alwagdani A, Alraddadi AA, Alamri A. Patterns of comorbidities in psoriasis patients: a cross-sectional study. *Cureus*. 2021;13(5):e14907. doi:10.7759/cureus.14907
6. Wu CY, Hu HY, Li CP, Chou YJ, Chang YT. Comorbidity profiles of psoriasis in Taiwan: a latent class analysis. *PLoS One*. 2018;13(2):e0192537. doi:10.1371/journal.pone.0192537
7. Chalitsios CV, Meena D, Manou M, et al. Multiple long-term conditions in people with psoriasis: a latent class and bidirectional Mendelian randomization analysis. *Br J Dermatol*. 2024;190(3):364–373. doi:10.1093/bjd/ljad410
8. Warrens MJ. On association coefficients for 2x2 tables and properties that do not depend on the marginal distributions. *Psychometrika*. 2008;73(4):777–789. doi:10.1007/s11336-008-9070-3
9. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2018. Available from: https://www.R-project.org/. Accessed June 30, 2024.
10. Kogan N, Veira R, Chaparro E, Crespo A, Gusis S, Hassan M. Comorbidities in psoriasis. *Psoriasis Forum*. 2010;16a(3):23–30. doi:10.1177/247553031016a00305
11. Duarte GV, Oliveira MF, Follador I, Silva TS, Carvalho Filho EM. Diagnosis and underdiagnosis of comorbidities in psoriasis patients - need for a multidisciplinary approach. *An Bras Dermatol*. 2016;91(6):743–747. doi:10.1590/abd1806-4841.20164716
12. Fatás-Lalana B, Cantón-Sandoval J, Rodríguez-Ruiz L, et al. Impact of comorbidities of patients with psoriasis on phototherapy responses. *Int J Mol Sci*. 2022;23(17):9508. doi:10.3390/ijms23179508
13. Zhang Y, Guo Y, Zhang K, et al. Comorbidities among adult patients with psoriasis in Tianjin: a cross-sectional analysis of the health database study. *BMJ Open*. 2024;14(5):e083683. doi:10.1136/bmjopen-2023-083683
14. Ng SK, Tawiah R, Sawyer M, Scuffham P. Patterns of multimorbid health conditions: a systematic review of analytical methods and comparison analysis. *Int J Epidemiol*. 2018;47(5):1687–1704. doi:10.1093/ije/dyy134
15. Potestio L, Tommasino N, Lauletta G, Martora F, Megna M. Psoriasis and molecular target therapies: evidence of efficacy in preventing cardiovascular comorbidities. *Dermatol Ther*. 2024;14(4):841–852. doi:10.1007/s13555-024-01152-w
16. Yan BX, Chen XY, Ye LR, Chen JQ, Zheng M, Man XY. Cutaneous and systemic psoriasis: classifications and classification for the distinction. *Front Med*. 2021;8:649408. doi:10.3389/fmed.2021.649408
17. Kaushik SB, Lebwohl MG. Psoriasis: which therapy for which patient: focus on special populations and chronic infections. *J Am Acad Dermatol*. 2019;80:43–53. doi:10.1016/j.jaad.2018.06.056
18. Daugaard C, Iversen L, Hjuler KF. Comorbidity in adult psoriasis: considerations for the clinician. *Psoriasis*. 2022;12:139–150. doi:10.2147/PTT.S328572

19. Yamazaki F. Psoriasis: comorbidities. *J Dermatol*. 2021;48(6):732–740. doi:10.1111/1346-8138.15840
20. Bunevicius R, Prange AJ. Thyroid disease and mental disorders: cause and effect or only comorbidity? *Curr Opin Psychiatry*. 2010;23(4):363–368. doi:10.1097/YCO.0b013e3283387b50
21. Song C, Ouyang F, Ma T, Gong L, Cheng X, Bai Y. Parental cardiometabolic multimorbidity and subsequent cardiovascular incidence in middle-aged adults: a prospective cohort study. *SSM Popul Health*. 2024;25:101634. doi:10.1016/j.ssmph.2024.101634
22. Fan J, Sun Z, Yu C, et al. Multimorbidity patterns and association with mortality in 0.5 million Chinese adults. *Chin Med J*. 2022;135(6):648–657. doi:10.1097/CM9.0000000000001985
23. Yang X, Zhang J, Chen S, Weissman S, Olatosi B, Li X. Comorbidity patterns among people living with HIV: a hierarchical clustering approach through integrated electronic health records data in South Carolina. *AIDS Care*. 2021;33(5):594–606. doi:10.1080/09540121.2020.1844864