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Daniel Z Lieberman

Roger Peele

Maryam Razavi

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## Combinations of DSM-IV-TR Criteria Sets for Bipolar Disorders

Daniel Z. Lieberman, M.D., Roger Peele, M.D., Maryam Razavi, M.D.

Department of Psychiatry and Behavioral Sciences

George Washington University

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Corresponding author:

Daniel Z. Lieberman, M.D

Department of Psychiatry and Behavioral Sciences

George Washington University

2150 Pennsylvania Ave, NW, Rm 8-421

Washington, DC 20037

Phone: (202) 741-2899

Fax: (202) 741-2891

Email: [dlieberman@mfa.gwu.edu](mailto:dlieberman@mfa.gwu.edu)

## Abstract

**Background:** DSM-IV-TR is the standard for making psychiatric diagnoses in many countries. The diagnostic categorization of DSM-IV-TR is valued for its reliability, however it is well-accepted that patients with the same diagnosis demonstrate substantial heterogeneity. In order to quantitatively characterize the degree of possible heterogeneity that can exist, combinatorial mathematics was used to calculate the number of possible ways to satisfy symptom criteria for the diagnosis of bipolar disorder as an example of this problem. **Sampling and Methods:** The formula  $n!/(r!(n-r)!)$ , which calculates the number of different ways of choosing an unordered number of items without repetition from a larger set, was used to calculate the number of combinations which meet the criteria for the core episodes of bipolar disorder and the specifiers. **Results:** The number of possible combinations for the core episodes ranged from 163 for a manic episode to 37,001 for a mixed episode. When the full collection of specifiers that DSM-IV-TR applies to bipolar disorder was used, the number of combinations was over five billion. **Conclusions:** The precision of medical communication about bipolar disorder is called into question by the billions of different ways that the criteria for this diagnosis can be met. As DSM-V is developed, the possible combinations for each diagnostic criteria should be calculated, and the effect this number has on clinical communication should be considered.

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## Introduction

The clarity and objectivity of a diagnostic system is central to the ability to study and treat medical illnesses. The DSM provides a framework for identifying discrete groups of mentally ill patients designed to permit evidence-based decisions regarding treatment selection, and accurate predictions regarding the course of the illness. Without reliable diagnostic definitions, communication about patients would be ambiguous, such that two clinicians might have very different conceptualizations of what is meant when using diagnostic labels, such as “depression,” for example.

Despite the advantages of the DSM taxonomy, it is understood that there remain serious deficiencies. One of these deficiencies is the variability that exists within diagnostic categories. For some disorders, DSM-IV-TR defines the disorder monothetically, e.g., hypochondriasis requires five of five characteristics. For other disorders, the definition is polythetic. For example, antisocial personality disorder requires only a subset of symptoms from a larger list, which allows for heterogeneous presentations of the disorder. Two patients could both meet the criteria for antisocial personality disorder without having any symptoms in common. The existence of this heterogeneity within the DSM structure is widely acknowledged, however the actual size of the variability may not be fully appreciated. Because the DSM is arguably the most important document in modern psychiatry, it is not enough to have an approximate understanding of the variability of diagnostic categories. A scientific approach requires a quantitative evaluation.

Enumerative combinatorics is a branch of combinatorial mathematics that can be used to calculate the number of ways of picking a certain number of items from a larger list of possibilities (1). The formula for calculating unordered combinations without repetition is symbolized by  $n!/r!(n-r)!$ , where  $n$  is the number of objects from which one can choose,  $r$  is the number to be chosen, and  $!$  is the standard symbol meaning “factorial.” We applied enumerative combinatorics to the DSM-IV-TR criteria for bipolar disorder as an example of the scope of diagnostic heterogeneity that exists within the current taxonomy. Bipolar disorder was selected to illustrate this aspect of the polythetic approach because it has many modifiers, and incorporates both depressive episodes and manic episodes. It was hypothesized that the number of ways in which a patient could satisfy the criteria would be large.

## Methods

Using the formula  $n!/r!(n-r)!$ , we calculated the number of possible combinations that would satisfy the DSM-IV-TR criteria for the following examples

- 1) Bipolar I Disorder, Single Manic Episode, with limited specifiers
- 2) Bipolar I Disorder, Most Recent Episode Mixed, with limited specifiers

### 3) Bipolar I Disorder, Most Recent Episode Depressed with and without catatonic, melancholic, and atypical features

Some of the criteria are compound, such that they include two, mutually exclusive symptoms. For example, both insomnia and hypersomnia are included within a single criterion of a major depressive episode. In order to simplify the mathematics, and increase the clarity of the results, these dual items were treated as a single choice. This decision led to a somewhat lower number of combinations.

The results were calculated by first determining the possible combinations for each component of a bipolar disorder diagnosis. For example, a major depressive episode requires either depressed mood or diminished pleasure plus four or more other symptoms. First the combinations were calculated for depressed mood plus four or more of eight other symptoms. The number of items in the list of possible choices was eight because a patient can have both depressed mood and diminished pleasure. The calculation was therefore: 4 of 8 = 70, 5 of 8 = 56, 6 of 8 = 28, 7 of 8 = 8, and 8 of 8 = 1. The total is 163. A patient with diminished pleasure requires an additional four or more of seven symptoms. The list of possible symptoms included only seven items in this calculation because the possibility of both depressed mood and diminished pleasure was included in the previous calculation. The calculation was therefore: 4 of 7 = 35, 5 of 7 = 21, 6 of 7 = 7, 7 of 7 = 1, totaling 64. Therefore the total number of combinations for the core criteria of a major depressive episode is 227.

Combining the components to obtain specific diagnoses involved multiplication. For example, because there are 227 ways to meet the criteria for a major depressive episode, and 163 ways to meet the criteria for a manic episode, there are 37,001 different possibilities for the two combined (i.e., bipolar I disorder, most recent episode mixed or bipolar I disorder, most recent episode depressed). The use of specifiers further increases the number of combinations. For example, the longitudinal course specifier increases the number of combinations by a factor of two. The severity/psychotic/remission specifier (representing the fifth digit in the numerical representation of the diagnosis) has six possible values. Because values 1, 2, 3, 5, and 6 (mild, moderate, severe, in partial remission, and in full remission) are partially related to the number of

symptoms present, we felt that their inclusion in the calculation would involve a certain amount of redundancy. Therefore we only counted two combinations for this specifier: psychotic or non-psychotic.

## Results

The total numbers of possible combinations of the components of the DSM-IV-TR bipolar disorder diagnoses are shown in Table 1. The mixed episode has the largest number of combinations because the criteria include a full manic and a full major depressive episode. Of the specifiers, the melancholic features specifier has the largest number of combinations based on the presence of two symptoms in criterion A, and a requirement of 3 or more symptoms out of a list of 6 in criterion B. Table 2 shows representative examples of full diagnoses, which include selected episodes and specifiers. None of the examples include both the atypical and melancholic specifiers together, since they are mutually exclusive.

## Discussion

Due to the system of categorization used by the DSM-IV-TR, in which diagnoses are arrived at by selecting a specified number of symptoms from a larger list, the number of different ways in which a patient can fulfill the criteria can be very large. The examples used to illustrate the magnitude of possible combinations range from 326 for a single manic episode with limited specifiers to over five billion when the complete set of specifiers are used.

There are several important caveats to note when interpreting the calculations. Not all of the symptom combinations are seen with equal frequency. If a particular presentation were rare, the combinations attributed to it would not reflect the actual variability seen in real populations. Calculations that considered actual symptom incidence might decrease the number of potential presentations. Not all of the symptoms are independent of one another. For example, many of the symptoms of the melancholia specifier overlap with the core symptoms of a depressive episode. Calculations that considered these overlaps would decrease the number of potential presentations.

These calculations assume that a patient with seven symptoms is different from a patient with only six, which may not be clinically relevant. Even if one takes the position, however, that only the minimum number of symptoms should be counted, there would still be a considerable number of combinations. For example, if only the minimum three symptoms are used in the calculation for a euphoric manic episode and only the minimum four symptoms for an irritable manic episode, there are still 70 possible combinations. If the minimum number of symptoms is regarded as adequate for a depressive episode, there are 105 different kinds of episodes, and the mixed episode would include 7,350 different manifestations. These figures do not include specifiers, which once again drive the number of combinations into the millions.

Another important consideration is whether patients who meet the bipolar disorder diagnostic criteria in different ways are experiencing significantly different pathophysiological disturbances. If the particular symptom combination that a patient experiences is arbitrary, it may not matter that there are billions of different ways to combine these symptoms into the same diagnosis. On the other hand, if individual symptoms are caused by specific neurobiological systems, the high degree of variability within the diagnosis becomes more relevant. Some aspects of the diagnosis may be more significant than others in terms of identifying distinct subgroups. For example, the presence or absence of psychotic features may be more relevant to classification than some of the other specifiers.

Suggestions for improving the performance of the DSM criteria include testing the psychometric properties of each of the criteria (2). The Rhode Island Methods to Improve Diagnostic Assessment and Services project focused on the criteria for major depressive disorder, and found that eliminating the somatic symptoms of depression would simplify the diagnosis, and help distinguish it from comorbid medical illnesses. They found a high level of concordance with the current criteria when the abbreviated criteria were used (3). Others have suggested the more fundamental change of replacing the categorical approach with a dimensional one (4).

Conclusion

Based on the DSM-IV-TR criteria set for the bipolar disorders, there are hundreds of millions to billions of different ways a single diagnosis can be expressed. This variability affects the precision of our communications about these disorders, and may lead to problems in identifying homogeneous populations for research studies. While it is not certain that a large number of combinations influences the practical utility of the DSM criteria sets, it is important to be aware of the magnitude of the number, especially when it reaches into the billions. We suggest that including this number in the text of the DSM that accompanies each diagnosis would lead to a greater appreciation of the heterogeneity associated with the criteria-defined approach.

#### References

1. Stanley RP: Enumerative Combinatorics. Cambridge, UK, Cambridge University Press, 1997
2. Zimmerman M, Chelminski I, McGlinchey JB, Young D: Diagnosing major depressive disorder VI: performance of an objective test as a diagnostic criterion. *J Nerv Ment Dis* 2006; 194(8):565-9
3. Zimmerman M, Chelminski I, McGlinchey JB, Young D: Diagnosing major depressive disorder X: can the utility of the DSM-IV symptom criteria be improved? *J Nerv Ment Dis* 2006; 194(12):893-7
4. Krueger RF, Piasecki TM: Toward a dimensional and psychometrically-informed approach to conceptualizing psychopathology. *Behav Res Ther* 2002; 40(5):485-99



Table 1. Total combinations of the components of the DSM-IV-TR bipolar disorder diagnoses.

<b>Episodes</b>	<b>Possible Combinations</b>
Major depressive episode	227
Manic episode	163
Hypomanic episode	163
Mixed episode	37,001
<b>Specifiers</b>	
Severity/psychotic/remission specifier	2
Chronic specifier	2
Catatonic features specifier	26
Melancholic features specifier	84
Atypical features specifier	11
Postpartum onset specifier	2
Longitudinal course specifiers	2
Seasonal pattern specifier	2
Rapid cycling specifier	2

Table 2. Examples of possible combinations of DSM-IV-TR signs and symptoms of bipolar disorders that fully addresses all of the specifiers.

Diagnosis	Combinations
Bipolar I, single manic episode, including only the severity specifier	326
Bipolar I, most recent episode mixed, without the inclusion of the catatonic, melancholic, or atypical specifiers	2,368,064
Bipolar I, most recent episode depressed, without the inclusion of the catatonic, or melancholic specifiers	26,048,704
Bipolar I, most recent episode depressed without the inclusion of the catatonic or atypical specifiers	198,917,376
Bipolar I, most recent episode depressed without the inclusion of the atypical specifier	5,171,851,776