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Latent class analysis for identifying subclasses of depression using JMP Pro 16

KARISHMA YADAV
Singapore Management University, karishmay.2020@mitb.smu.edu.sg

Fei Fei Sue-ann SEET
Singapore Management University, feifei.seet.2020@mitb.smu.edu.sg

Tin Seong KAM
Singapore Management University, tskam@smu.edu.sg

Tin Seong KAM

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The Use of Latent Class Analysis for Identifying Subclasses of Depression: JMP Pro Method

Karishma Yadav, Sue-Ann SEET, Yi Ying TAN, Tin Seong KAM; Singapore Management University

ABSTRACT

According to WHO, "Depression is a leading cause of disability worldwide and is a major contributor to the overall global burden of disease". A major stumbling block in the care of depressed patients remains the accurate diagnosis of the severity of depression.[1] Patient Health Questionnaire (PHQ-9), a 9-question instrument is widely used for diagnosing and determining the severity of depression. However, the popularly used 5-Category of depression severity based on the sum of responses to the 9 questions was overly subjective. In view of this limitation, our paper aims to demonstrate how Latent Class Analysis of JMP Pro can be used to provide a data-driven and objective approach to determine depression severity classes. The study was conducted using Mental Health-Depression Screener from National Health and Nutrition Examination Survey (NHANES) 2017-2018, conducted by the Centers for Disease Control and Prevention, USA. The analysis results reveal that Latent Class Analysis improves our understanding of the characteristics of depression classes better than conventional 5-Category method.

INTRODUCTION

A. PHQ-9

The Patient Health Questionnaire-9 (PHQ-9) also known as Mental Health - Depression screener, is typically administered to determine the frequency of depression symptoms over the past 2 weeks. It uses a total of 9 questions which focus on symptoms of depression, each question results in a response ranging from 0 to 3 (0-None of the days to 3-Almost every day). Sum of responses of all the 9 questions is used to calculate the PHQ-9 score, ranging from 0 to 27. From a clinical standpoint, PHQ-9 has been assessed to be a valid instrument of measuring severity of depression.[2]

Below is the list of questions that make PHQ-9:

1. Have little interest in doing things
2. Feeling down, depressed, or hopeless
3. Trouble sleeping or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself
7. Trouble concentrating on things
8. Moving or speaking slowly or too fast
9. Thought you would be better off dead

Introduced in 2002 by Kroenke and Spitzer, the PHQ-9 was developed to provide an alternative depression diagnostic measure that is simpler to administer compared to current and prior measures developed. The PHQ-9 has since been used as a common questionnaire in clinical and research setting to diagnose and determine the severity of depression. However, from a statistical analysis point of view, the PHQ-9 scoring system appears to be too simplistic as it simply takes the sum of response variables and defines strict cut points to assess the severity of depression. As such, the need for analysis to be conducted using statistical methods such as clustering to identify clusters within the population will enable a clearer understanding of depression classes.

B. Research objective

In this study, we build upon the strengths of PHQ-9 questionnaire which has reproduced high reliability and efficiency scores in clinical settings (Kroenke & Spitzer, 2001). Using the same set of 9 questions taken from the Questionnaire Data set of NHANES 2017-2018, 5,068 respondents were classified into depression severity classes using latent class analysis. At the same time, mere summation of response variables to arrive at the severity levels for depression using PHQ-9 cut points was questioned by comparing PHQ-9 severity levels with the clusters obtained using Latent Class Analysis in JMP Pro 16 using Contingency Table Analysis.

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[1] World Health Organisation Depression Factsheet, https://www.who.int/news-room/fact-sheets/detail/depression

[2] Validity of the PHQ-9, a brief depression severity measure https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495268/

The contribution of this paper:

- The use of Mental Health-Depression Screener dataset to classify respondents into depression severity classes using LCA will reveal the contribution of each response variable to the severity cluster. And this will help in the identification of optimal method for assessing the PHQ-9 response sheet.
- The comparison of clusters obtained from the LCA method with the widely and clinically defined severity levels in the PHQ-9 using the Contingency Table Analysis will reveal differences in the severity of depression classes between the two. The data-driven approach to identify clusters will help clinicians to come up with a more suitable method to assess the severity of depression.

C. Paper outline

In the next sections, the paper will first review the literature related to this study, followed by the data preparation and methodology of the study. Subsequently, the paper will discuss the latent class analysis and the contingency table analysis results. Further insights will be illustrated before concluding the paper.

LITERATURE REVIEW

Since its inception in 2001, the PHQ-9 questionnaire has been widely used in research studies surrounding the topic of depression, depression screening, depression subgrouping and related topic areas. Studies have also looked at ways to apply the PHQ-9 depression screener to actual data sets, such as –to compare across depression treatments (McMillan, Gilbody & Richards, 2010 or as a tool for gauging response to pharmacological treatment (Löwe et al, 2006). However, these studies largely focused on the clinical usage of PHQ-9. Limited studies utilize statistical analysis methods like cluster analysis to assess the severity classes defined in PHQ-9. Inevitably, diagnosing and determining severity of depression have been challenging tasks for decades for practitioners and clinical researchers due to the lack of standardization pertaining to depression symptoms, behaviors, and severity classes for analysis purposes. In one study, it was found that out of the 9 questions in the PHQ-9, one of the questions was able to identify patients with increased risk of suicide attempt (Simon, Rutter et al., 2013). Other analyses have been done to explore depression subtypes which could be identified through latent class analysis based on depression symptoms (Ulbricht et al., 2018). However, results showed that no consistent set of depression subtypes were formed because prior models built were based on different observed indicators. Therefore, using statistical analysis in the widely adopted PHQ-9 could potentially bring about a consistent method to extract depression subgroups across various data sets.

DATA PREPARATION

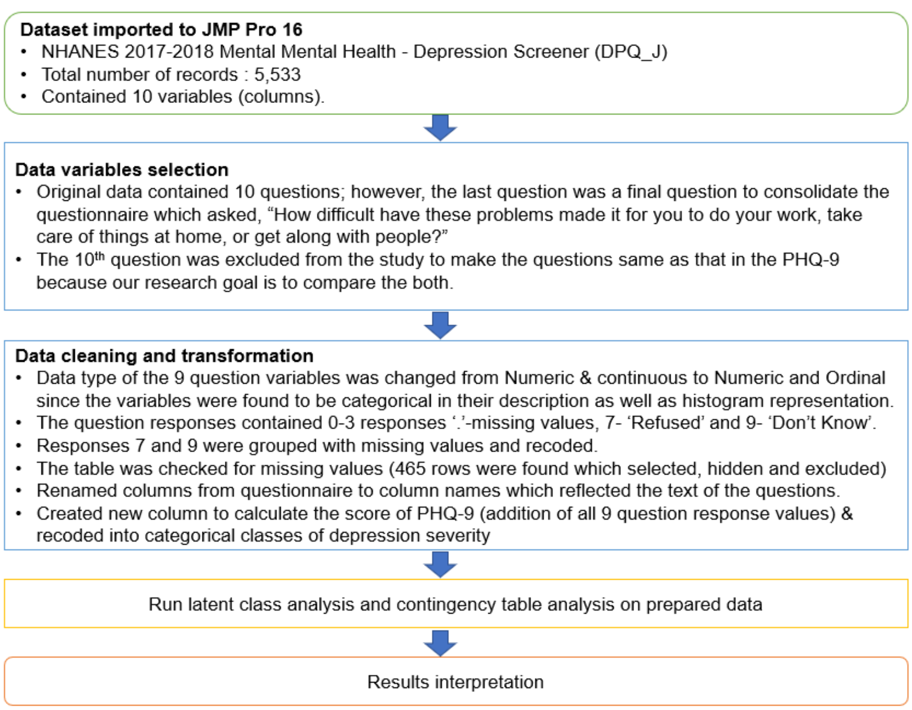

Figure 1: Data preparation flow

Firstly, the publicly available Mental-Health Depression Screener dataset was downloaded from the NHANES 2017 – 2018, Questionnaire data set. 1 survey data was used to maintain the data quality of the survey results without conflating possible differences the way respondents answer a survey over different time periods.

As shown in Figure 1 above, the dataset (2017-2018) was prepared using JMP Pro 16 as the analytical toolkit for this study. In the dataset, there were a total of 10 columns, with DPQ100 recording a response to the question – "How difficult have these problems made it for you to do your work, take care of things at home, or get along with people?". As this final question is not part of the PHQ-9 measure, it was removed. Data cleaning and preparation was done such as checking for missing values, renaming columns to reflect variables for later analysis. For each of the 9 variables, the data type was updated from Numeric and continuous to type: Numeric and Ordinal for latent class analysis to be done. The PHQ-9 score was also tabulated in a new column (PHQ-9 score) and recoded into the 5-categories of depression severity, namely – None, Mild, Moderate, Moderately Severe and Severe. The final list of variables can be found in Appendix A.

To validate our analysis, NHANES 2007-2008 was also downloaded, and same analysis was done on it, to eliminate time difference and generalize our analyses results irrespective of time.

METHODOLOGY

This section lays out the sequential steps of the statistical analyses performed. First, JMP Pro 16 was used to conduct latent class analysis (LCA) to group the interviewed individuals with distinct patterns into clusters. The best clustering model was selected based (smallest) BIC and AIC values. From the model reports, the effect sizes of respective variables were evaluated to identify the separation between latent classes, which indicate the accuracy of categorizing individuals to the correct latent class. The LogWorth values are also examined to determine the influence of each variables on the model.

Next, contingency table analysis was carried out to compare LCA clusters to the 5-categories of depression severity classes derived using PHQ-9. Our hypothesis is that the popularly used PHQ-9 method based on the sum of responses is overly subjective, as it does not consider the statistical weightage of individual variables. Comparing this to the LCA results that is populated using statistical methods will allow us to examine the validity of the PHQ-9 results.

FINDINGS AND DISCUSSIONS

A. Latent Class Analysis

LCA was run choosing the 9 questions as Y variables for range of clusters from 3 to 15 as shown in figure 2. The best clustering model is the one that has the smallest BIC and AIC values. However, given the smallest AIC could not be achieved on this dataset (the AIC gets smaller as the number of clusters increases), Cluster 5 that had the smallest BIC was found to be the optimal cluster size.

Cluster Comparison

NCluster	-LogLikelihood	BIC	AIC	Best
3	27231.3	55170.7	54628.6	
4	26946.8	54840.6	54115.7	
5	26745.1	54676	53768.3	Smallest BIC
6	26626.3	54677.3	53586.7	
7	26550.4	54764.3	53490.8	
8	26490.6	54883.6	53427.3	
9	26434.5	55010.1	53370.9	
10	26378.1	55136.2	53314.1	
11	26330.3	55279.4	53274.5	
12	26289.8	55437.3	53249.5	
13	26250.4	55597.5	53226.9	
14	26214.5	55764.5	53211	
15	26180.3	55935	53198.7	Smallest AIC

Figure 2: Results of latent class analysis

The tables below set out the cluster response percentage within variables and the cluster response probability across levels of each variables.

Table 1: Cluster response percentage within variables

	Cluster 1 None	Cluster 2 Mild	Cluster 3 Moderate	Cluster 4 Moderately Severe	Cluster 5 Severe
Class Size	**0.48**	**0.24**	**0.11**	**0.10**	**0.06**
Indicators					
Have little interest in doing things					
Not at all	0.96	0.76	0.63	0.18	0.11
Several days	0.02	0.21	0.16	0.70	0.20
More than half the days	0.01	0.02	0.14	0.11	0.32
Nearly every day	0.01	0.01	0.07	0.02	0.37
Feeling down, depressed or hopeless					
Not at all	0.98	0.82	0.71	0.06	0.03
Several days	0.02	0.17	0.14	0.82	0.20
More than half the days	0.00	0.00	0.11	0.12	0.33
Nearly every day	0.00	0.00	0.05	0.01	0.45
Trouble sleeping or sleeping too much					
Not at all	0.90	**0.45**	**0.37**	0.23	0.09
Several days	0.07	0.49	0.12	0.45	0.19
More than half the days	0.02	0.03	0.25	0.18	0.20
Nearly every day	0.01	0.03	0.26	0.13	0.52
Feeling tired or having little energy					
Not at all	0.87	**0.23**	**0.19**	0.08	0.04
Several days	0.10	0.73	0.22	0.58	0.13
More than half the days	0.02	0.02	0.33	0.23	0.24
Nearly every day	0.01	0.02	0.26	0.12	0.60
Poor appetite or overeating					
Not at all	0.96	0.70	**0.55**	0.37	0.25
Several days	0.03	0.27	0.15	0.46	0.18
More than half the days	0.01	0.03	0.15	0.12	0.25
Nearly every day	0.00	0.01	0.14	0.05	0.33
Feeling bad about yourself					
Not at all	0.99	0.87	0.85	0.37	0.16
Several days	0.01	0.13	0.08	0.50	0.30
More than half the days	0.00	0.00	0.05	0.10	0.21
Nearly every day	0.00	0.00	0.02	0.03	0.32
Trouble concentrating on things					
Not at all	0.98	0.84	0.77	0.51	0.28
Several days	0.01	0.15	0.11	0.35	0.17
More than half the days	0.00	0.01	0.06	0.10	0.20
Nearly every day	0.00	0.00	0.07	0.04	0.34
Moving or speaking slowly or too fast					
Not at all	0.99	0.84	0.84	0.67	0.41
Several days	0.00	0.07	0.07	0.25	0.23
More than half the days	0.00	0.05	0.05	0.06	0.16
Nearly every day	0.00	0.03	0.03	0.02	0.21
Thought you would be better off dead					
Not at all	1.00	0.99	0.97	0.89	0.64
Several days	0.00	0.01	0.02	0.10	0.22
More than half the days	0.00	0.00	0.01	0.01	0.09
Nearly every day	0.00	0.00	0.01	0.00	0.06

The characteristics of the clusters were examined, and it was found that Cluster 1 was the biggest cluster with 48% of the sample size and Cluster 5 was the smallest with 6% of the sample size (Table 1). Approximately 90% of the individuals in Cluster 1 responded that they do not experience any depression symptoms. In Cluster 2, the individuals experienced 2 out of the 9 symptoms for having trouble sleeping or sleeping too much and feeling tired, In Cluster 3, on top of the depression symptoms experienced by those in Cluster 2, the individuals experienced poor appetite or overeating for several days in a week in the past year. It was observed that the number of depression symptoms experienced by individuals increased from Cluster 1 to Cluster 5. Detailed description of the cluster analyses can be found in Table 2 below.

The number of symptoms and their respective levels indicate scoring results like the depression severity based on PHQ-9 score hence we assigned them the same category names - None, Mild, Moderate, Moderately Severe and Severe.

Table 2: Description of the LCA clusters

Cluster No	Name	Description
1	None	The class size is 48%. Individuals in this group do not experience any depressive symptoms at all. No risk of experiencing depression.
2	Mild	Representing 24% of the sample size. The group experience 2 out of 9 of the depressive symptoms, have trouble sleeping or sleep too much several days in a week, as well as feel tired or have little energy several days in a week.
3	Moderate	Representing 11% of the sample size. Majority (71%) in this group feel tired or have little energy at least several days a week. More than half in this group feel tired more than half the week or daily. It can be seen in Section B below that feeling tired is one of the key variables that have the strongest influence in the model. The group are also experiencing increased number of days in (10-20% shift from not at all to several days a week): • Have little interest in doing things • Feeling down, depressed, or hopeless • Trouble sleeping or sleeping too much
4	Moderately Severe	The class size is 10%. Bigger group of individuals in this cluster experience several days in a week (50-80%) the same symptoms experienced by the individuals of Group 3. On top of that they feel bad about themselves and have trouble concentrate on things several days a week. The group are having 7 out of 9 of the depressive symptoms.
5	Severe	Representing 6% of the sample size. The group experience the same symptoms of those faced by the moderately severe group but with higher frequencies. Instead of experiencing for just several days a week they have that nearly every day or more than half the days. There is also increasing trend of individuals who experience 2 more depressive symptoms: • Moving or speaking slowly or too fast • Thought you would be better off dead At this stage 20% of the group are having 9 out of 9 of the depressive symptoms.

Table 3: Cluster response probability across levels of each variables

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
	None	Mild	Moderate	Moderately Severe	Severe
Class Size	0.48	0.24	0.11	0.10	0.06
Indicators					
Have little interest in doing things					
Not at all	0.62	0.25	0.09	0.03	0.01
Several days	0.05	0.31	0.11	0.45	0.07
More than half the days	0.07	0.10	0.30	0.20	0.33
Nearly every day	0.14	0.07	0.20	0.04	0.54
Feeling down, depressed or hopeless					
Not at all	0.62	0.26	0.10	0.01	0.00
Several days	0.06	0.26	0.09	0.52	0.07
More than half the days	0.02	0.00	0.27	0.28	0.42
Nearly every day	0.01	0.03	0.16	0.02	0.79
Trouble sleeping or sleeping too much					
Not at all	0.71	0.18	0.07	0.04	0.01
Several days	0.15	0.53	0.06	0.21	0.05
More than half the days	0.11	0.11	0.38	0.25	0.15
Nearly every day	0.08	0.09	0.33	0.15	0.34
Feeling tired or having little energy					
Not at all	0.83	0.11	0.04	0.02	0.00
Several days	0.15	0.56	0.08	0.19	0.02
More than half the days	0.11	0.06	0.42	0.26	0.15
Nearly every day	0.07	0.05	0.34	0.14	0.40
Poor appetite or overeating					
Not at all	0.62	0.23	0.08	0.05	0.02
Several days	0.08	0.42	0.11	0.31	0.07
More than half the days	0.06	0.14	0.32	0.23	0.26
Nearly every day	0.03	0.04	0.37	0.13	0.43
Feeling bad about yourself					
Not at all	0.57	0.25	0.11	0.05	0.01
Several days	0.03	0.28	0.08	0.46	0.15
More than half the days	0.02	0.01	0.19	0.36	0.42
Nearly every day	0.00	0.04	0.08	0.13	0.76
Trouble concentrating on things					
Not at all	0.57	0.25	0.10	0.06	0.02
Several days	0.07	0.35	0.12	0.36	0.10
More than half the days	0.02	0.05	0.21	0.35	0.37
Nearly every day	0.06	0.03	0.22	0.11	0.58
Moving or speaking slowly or too fast					
Not at all	0.54	0.25	0.11	0.08	0.03
Several days	0.03	0.24	0.13	0.40	0.20
More than half the days	0.05	0.09	0.24	0.25	0.38
Nearly every day	0.00	0.03	0.21	0.13	0.64
Thought you would be better off dead					
Not at all	0.50	0.25	0.11	0.10	0.04
Several days	0.01	0.06	0.08	0.40	0.46
More than half the days	0.00	0.03	0.10	0.08	0.78
Nearly every day	0.04	0.00	0.18	0.00	0.78

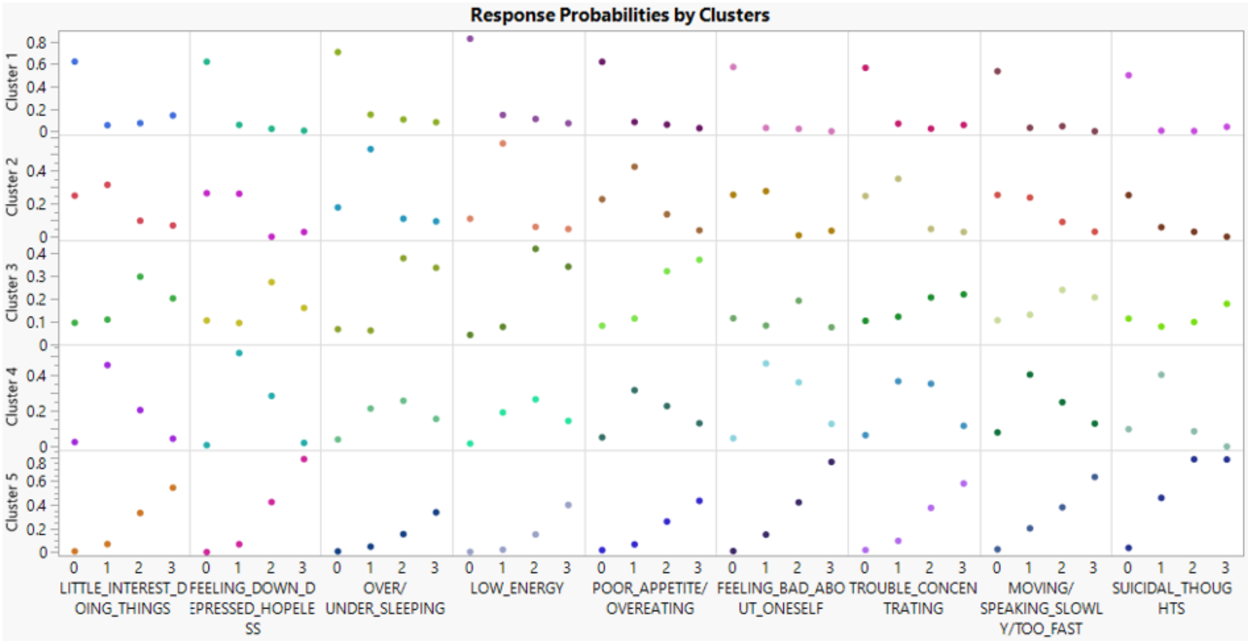

Figure 3: Graphical display of response probabilities by Clusters

Finally, the probability of each response categories across the clusters was examined. LCA is model-based and provides information about the maximum likelihood that an individual belongs to a certain cluster.

It can be seen from Table 3, for example, among the response of feeling down or depressed nearly every day, 79% are from Cluster 5, 2% are from Cluster 4, 16% are from Cluster 3, 3% are from Cluster 2 and 1% are from Cluster 1. The percentage should sum up to 100% if we move horizontally across the table.

B. Effect Sizes and LogWorths in LCA

Effect Sizes

Column	Effect Size	LR LogWorth
LITTLE_INTEREST_DOING_THINGS	0.8108	551.15
FEELING_DOWN_DEPRESSED_HOPELESS	0.9766	752.62
OVER/UNDER_SLEEPING	0.7699	570.46
LOW_ENERGY	0.9448	865.96
POOR_APPETITE/OVEREATING	0.6776	426.35
FEELING_BAD_ABOUT_ONESELF	0.7821	462.17
TROUBLE_CONCENTRATING	0.6564	333.14
MOVING/SPEAKING_SLOWLY/TOO_FA...	0.5631	237.5
SUICIDAL_THOUGHTS	0.4785	125.21

Figure 4: Effect Sizes in LCA

Based on the Cluster 5 statistical details given in Table 2, the effect size per input variable and its corresponding LogWorth values are shown in Figure 3.

The effect size values are between 0 and 1. The higher effect size indicates the higher likelihood of individuals being classified accurately in a latent class. Majority of the input variables have high effect sizes of >75%. The few variables with lower effect size hence lower distinction between groups are:

1. Poor appetite or overeating
2. Trouble concentrating on things
3. Moving or speaking slowly or too fast
4. Thought you would be better off dead

LogWorth, on the other hand, is the effectiveness of the variables in predicting the clusters. The larger the LogWorth, the stronger the variable in the model. The results indicate that not all variables share the same LogWorth values, each of them contributes different weight to the model and this will strongly challenge the summation of PHQ-9 scores to derive the depressive symptoms. Summation of PHQ-9 score will only be accurate and reliable if each variance has the same level of influence in the model. Among the variables that have stronger influence in this Cluster 5 model are:

1. Feeling tired or having little energy
2. Feeling down, depressed, or hopeless

Variables that have weaker influence in the model are:

1. Thought you would be better off dead
2. Moving or speaking slowly or too fast
3. Trouble concentrating on things

C. Contingency Analysis of Most Likely Clusters by Depressive Symptoms

After the examination of the LCA clusters, its resultant clusters were compared to those derived using PHQ-9. We performed a contingency analysis by fitting the depressive symptoms by the most likely clusters.

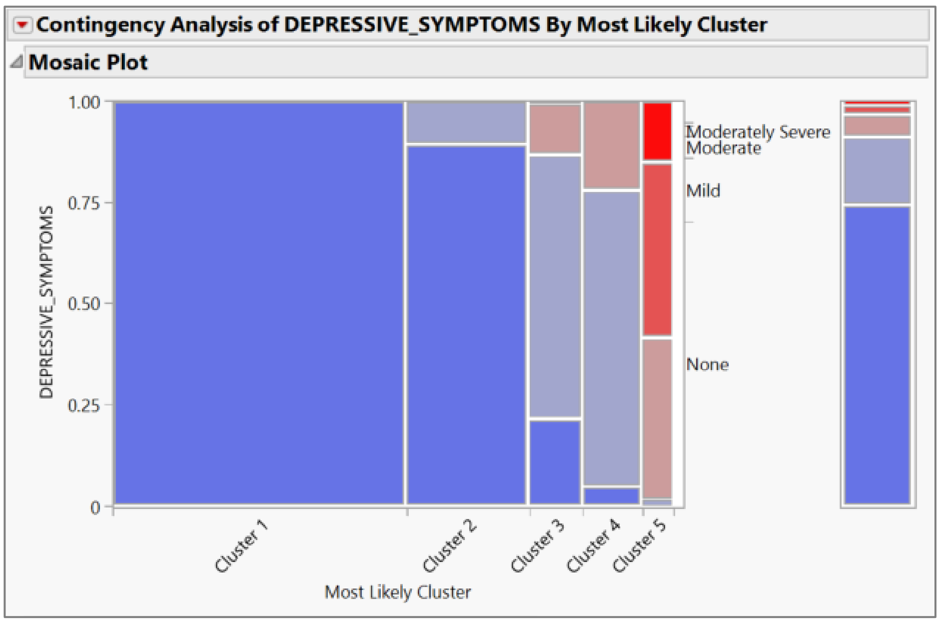

Figure 5: Contingency Analysis of Depressive Symptoms (Using PHQ-9) Vs Most Likely Cluster (using LCA)

Contingency Table

DEPRESSIVE_SYMPTOMS

Most Likely Cluster	Count Total % Col % Row %	None	Mild	Moderate	Moderately Severe	Severe	Total
Cluster 1		2656	0	0	0	0	2656
		52.41	0.00	0.00	0.00	0.00	52.41
		70.41	0.00	0.00	0.00	0.00	
		100.00	0.00	0.00	0.00	0.00	
Cluster 2		984	119	0	0	0	1103
		19.42	2.35	0.00	0.00	0.00	21.76
		26.09	14.22	0.00	0.00	0.00	
		89.21	10.79	0.00	0.00	0.00	
Cluster 3		105	319	62	2	0	488
		2.07	6.29	1.22	0.04	0.00	9.63
		2.78	38.11	21.23	1.61	0.00	
		21.52	65.37	12.70	0.41	0.00	
Cluster 4		27	394	118	0	0	539
		0.53	7.77	2.33	0.00	0.00	10.64
		0.72	47.07	40.41	0.00	0.00	
		5.01	73.10	21.89	0.00	0.00	
Cluster 5		0	5	112	122	43	282
		0.00	0.10	2.21	2.41	0.85	5.56
		0.00	0.60	38.36	98.39	100.00	
		0.00	1.77	39.72	43.26	15.25	
Total		3772	837	292	124	43	5068
		74.43	16.52	5.76	2.45	0.85	

Tests

N	DF	-LogLike	RSquare (U)
5068	16	2616.5179	0.6351

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	5233.036	<.0001*
Pearson	7084.359	<.0001*

Figure 6: Contingency Analysis of depressive symptoms by most likely clusters

Table 4: Tabulated results of contingency analysis

Depressive Symptoms	PHQ-9 (%)	LCA Clustering (%)
None	74.43	52.41
Mild	16.52	21.76
Moderate	5.76	9.63
Moderately Severe	2.45	10.64
Severe	0.85	5.56

From Table 4, it can be concluded that using PHQ-9 results, the derived percentages of individuals' depression severities are very different from those in the LCA analysis. The classification done by adding the responses of PHQ-9 indicates that 74% of individuals are in the no risk group whereas the classification using LCA statistical model indicates that only 52% of individuals have no risk. PHQ-9 shows that 16.52% of individuals have mild depressive symptoms but LCA shows 21.76% in this group. For all classifications with higher severity (from mild to severe), using the PHQ-9 measure consistently gives us a lower percentage as compared to LCA.

This means that individuals' depression severities are underestimated using PHQ-9 cut-points. The population of individuals who are potentially depressed is also underestimated. The p-value is examined to ensure that there is no sampling error. The model is showing p-value of <0.0001, we can conclude that there is a statistically significant association between the variables.

D. *Impact of Misclassifications using PHQ-9*

Underestimating the depression severities of individuals and the percentage of depressed population imposes significant risk to the society. Without an accurate diagnosis method, it becomes difficult to determine the adequate resources required to prevent and treat depressions.

Prevention programs are proved to be effective in reducing depression. Different kind of community programs can be designed to meet the needs of different groups. For example, school-based programs are effective to instill positive thinking patterns among schooling children and adolescents. Whereas exercise programs can be rolled out to prevent depression among elderlies. The need of such programs will most likely be underestimated if PHQ-9 severity levels are used to determine individuals' depression severity.[3]

The inaccurate PHQ-9 diagnosis will also impact the treatments of depression. Different severity of depressions requires different treatments. If healthcare providers cannot determine the right level or right kind of treatment, they will not be able to treat the patients effectively. Hence, it is suggested that clinicians develop a statistically derived scale such as the clusters derived in this study, to assign depression severity levels to patients.

CONCLUSIONS AND FUTURE WORKS

The findings of this study show that depression severity levels derived using statistical clustering models like LCA will provide more accurate assessment of depression severity compared to those derived using mere summation of responses of the PHQ-9. The same analysis was also carried out on NHANES 2007-2008 dataset and the results were found to be consistent eliminating the factor of time. Further studies need to be done to determine the weightage of the respective variables to strengthen the PHQ-9 model that has proved to be reliable and efficient.

APPENDIX A

Original Variable name	Final variable name	Data Type, Modelling type	Description
DPQ010	LITTLE_INTEREST_DOING_THINGS	Numeric, Ordinal	From original data
DPQ020	FEELING_DOWN_DEPRESSED_HOPELESS	Numeric, Ordinal	From original data
DPQ030	OVER/UNDER_SLEEPING	Numeric, Ordinal	From original data
DPQ040	LOW ENERGY	Numeric, Ordinal	From original data
DPQ050	POOR APPETITIE/OVEREATING	Numeric, Ordinal	From original data
DPQ060	FEELING_BAD_ABOUT_ONESELF	Numeric, Ordinal	From original data
DPQ070	TROUBLE_CONCENTRATING	Numeric, Ordinal	From original data
DPQ080	MOVING/SPEAKING_SLOWLY/TOO_FAST	Numeric, Ordinal	From original data
DPQ090	SUICIDAL_THOUGHTS	Numeric, Ordinal	From original data
DPQ100	•	•	Removed from this study
-	PHQ-9 SCORE	Numeric, Ordinal	Calculated from original date responses
-	DEPRESSIVE_SYMPTOMS	Character, Ordinal	Recoded from PHQ-9 score

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CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Name: Karishma YADAV
E-mail: karishmay.2020@mitb.smu.edu.sg

Name: Sue-Ann SEET
E-mail: feifei.seet.2020@mitb.smu.edu.sg

Name: Yi Ying TAN
E-mail: yiying.tan.2020@mitb.smu.edu.sg