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Identify the latent class of modifiable risk behaviours among diabetic and hypertensive patients in Northeast India: a population-base cross-sectional study

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Identify the latent class of modifiable risk behaviours among diabetic and hypertensive patients in Northeast India: a population-base cross-sectional study

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MeSh Keywords:

Type 2 Diabetes ; Hypertension, Alcohol Drinking, Smoking; Latent Class Analysis.

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Abstract

Objective: To identify the latent class of modifiable risk factors among the diabetic and hypertensive patients based on the observed indicators variables: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. It is hypothesized that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Design: A cross-sectional study was conducted using the national representative large scale survey data.

Setting and participants: The data comes from the Indian National Family Health Survey (NFHS-4), 2015-16. Participants aged 15-49 years who were diagnosed with either diabetes or hypertension, or both were included. The total sample is 22,249, out of which 3,284 were males, and 18,965 were females.

Primary and secondary outcome measures: The observed variables used as latent indicators are: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. The concomitant variables include age, gender, education, marital status, and household wealth index. Latent class model was used to simultaneously identify the latent class and to determine the association between the concomitant variables and the latent class.

Results: Three latent classes were identified and labelled as Class 1: "Diabetic with low-risk lifestyle" (21%), Class 2: "High-risk lifestyle" (8%), and Class 3: "Hypertensive with low-risk lifestyle" (71%). Class 1 had a high probability of having diabetes and low probability of smoking and drinking alcohol. Class 2 respondents were characterized by high probability of smoking and drinking alcohol and Class 3 is characterized by high probability of having high blood pressure and low probability of smoking and drinking alcohol.

Conclusions: Male should manage smoking and alcohol consumption, while females should control body weight and blood pressure. Marital status and gender could be the preventive factors for high-risk smoking and alcohol drinking in Northeast India

Keywords: Modifiable risk; Diabetes; Hypertension; Latent class analysis; Northeast India.

Strengths and limitations of the study

- The sample for the study is relatively large as it used nationally representative largescale data.
- Respondents' status of diabetes and hypertension is diagnosed using the biomarker measurement.
- Latent class analysis is a person-centred technique and the appropriate method for explaining the clustering of health risk behaviours.
- > The cross-sectional design of the study restricts us to measure the causal effect.
- Modifiable risk factors were collected based on dichotomous response which limits us to measure the intensity of substance use.

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Introduction

Effective lifestyle modification plans and affordable approaches to control high blood sugar and high blood pressure level would benefit the at-risk population [1,2]. The leading causes of mortality due to chronic disease in adults, particularly older adults, are linked to unhealthy lifestyle and behaviours [3], like tobacco consumption, physical inactivity, excess alcohol consumption, and poor diet. Usually, most risk behaviours exist simultaneously or cluster within individuals [4]. It is argued that lifestyle risk factors within individuals are not random but more likely to cluster with other unhealthy behaviours [5,6]. In Asia, for example, almost 43.5% of Chinese adults and 37% of Korean adults had at least two cardiovascular risk factors [4,7]. Moreover, in India, 35.64% of adult men and 10% of adult women had at least three lifestyle risk factors [8].

Latent Class Analysis (LCA), based on structural equation modelling, is a personcentred analytical approach that allows the identification of homogeneous sub-groups in a heterogeneous population. LCA is similar to cluster analysis because individuals are classifying into homogenous unobserved (latent) groups based on the response pattern to a set of observed variables. However, in cluster analysis, objects are classified based on distance measures, whereas in LCA classification are based on probabilistic and finite mixture modelling approach [9,10]. A latent class model splits the population into mutually exclusive and exhaustive groups that are homogeneous within the groups but differ among them. Several studies have adopted the LCA approach to identify risk factors clustering within the heterogeneous population. In a study by Dey et al, based on seven observed risk factors, LCA was used to classify individuals into two latent class "susceptible to adverse health outcomes groups" and "not susceptible to adverse health outcomes groups" [11]. Another study from China applied LCA to ten observed complications and comorbidities of T2 diabetic patients and categorized the individuals into four latent classes, namely "complications and comorbidity groups", "high risk of complications group", "high risk of comorbidities and Cardio Vascular Disease groups", and "diabetes without complications and comorbidities group" [12]. A study in West Azerbaijan province among the hypertensive patients aged 50 years and above used four indicators such as dietary patterns, physical activity, tobacco use, and high blood pressure control to categorized the hypertensive patients into three latent classes [13].

The majority of studies reported a higher prevalence of smoking, excess alcohol consumption, physical inactivity, and poor diet among people with diabetes or hypertension

than those without diabetes or hypertension [14,15]. Notably, previous studies have examined diabetic or hypertensive patients as a single homogeneous group without considering the possible heterogeneity existing within the population [16]. Identifying the clustered pattern of modified risk factors for diabetes and hypertension and the socio-demographic factors associated with clusters of unhealthy lifestyle behaviours allows health intervention program to target these risk factors simultaneously and effectively.

Most of the existing studies on health risk behaviours have emphasized only changing a single unhealthy behaviour [15,17]. However, interventions that simultaneously targets these unhealthy behaviours are necessary from the policy point of view [4]. In addition, existing studies in India on clustering of Non Communicable disease (NCD) risk factors have used intraclass correlation and scoring methods [8,18,19]. However, studies have suggested that LCA is the most appropriate method for explaining the clustering of health risk behaviours [20,21]. LCA is a probabilistic model approach designed for identifying clusters based on dichotomous variables. This study is the first in Northeast India to explore the clustering of NCD risk factors using the LCA approach. This study aims to identify the latent class of modifiable risk factors among diabetic and hypertensive patients based on the observed indicators variables: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. We applied LCA to investigate heterogeneity in the population of an individual with diabetes and hypertension and to identify possible latent class based on the response of observed risk factors. More specifically, the objective is to describe how individuals in Northeast India diagnosed with diabetes or hypertension are clustered according to the pattern of observed risk factors and identify the difference between these groups based on sociodemographic characteristics. We hypothesize that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Methods

Study location

The study focuses on the Northeastern region of India comprising eight states, namely Assam, Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, and Tripura (Figure 1). The region has a hilly terrain inhabited mainly by tribal people belonging to different cultures and ethnic communities [22]. It has over 45 million, which is 3.76% of India population and a population density of 159 persons per square km [23].

Figure 1: Map showing the location of the Study area

Design

A cross-sectional study was conducted using the national representative large scale survey data. The analysis is based on the publicly available secondary data where the identification of respondent is concealed [24].

Setting

The data comes from the fourth round of the Indian National Family Health Survey (NFHS-4) conducted during the year 2015-16. The data was downloaded from the DHS website [25]. NFHS was initiated by the Ministry of Health and Family Welfare, Government of India, and coordinated by the International Institute for Population Sciences, Mumbai. The survey adopted a stratified two-stage sampling design. In the first stage, primary sampling units (PSUs) were selected based on probability proportional to population size. Rural PSUs were villages, while census enumeration blocks formed the PSUs in urban areas. In the second stage, systematic random sampling was done in each PSUs to select households for the sample. At the household level, information was sought from the women aged 15 - 49 years and men aged 15 - 54 years. A detailed description of the survey design can be found elsewhere [24].

Sample

The study consists of individuals aged 15-49 years who were diagnosed with either diabetes or hypertension, or both. The total sample size is 22,249, out of which 3,284 were males, and 18,965 were females.

Patient and Public Invlovement

No patient involved

Measures

Diabetes: Fingerstick blood is collected, and blood glucose level is determined using the FreeStyle Optium H Glucometer. Respondent is considered diagnosed with diabetes if the random blood sugar level is >140mg/dl [24].

Hypertension: Blood pressure level was measured using an OMRON Blood Pressure measuring device. Three separate blood pressure readings were taken with an interval of 5 minutes between readings. A respondent is considered hypertensive if the systolic blood

pressure \geq 140 mmHg, or diastolic blood pressure \geq 90 mmHg, or if the respondent was taking antihypertensive medication to lower blood pressure at the time of the survey [24].

Overweight or obesity: In this study, we categorized continuous body mass index (BMI) according to the WHO guidelines for the Asian population. A respondent was classified as overweight or obese if $BMI \ge 23 \text{ kg/m}^2$ [26].

Outcome Variables of Interest

Observed Indicators variables: The observed variables used as latent indicators are cigarette's smoking (No=1, Yes=2), Alcohol consumption (No=1, Yes=2), Takes aerated drink (No=1, Yes=2), Overweight or obesity (No=1, Yes=2), Diabetes (No=1, Yes=2), Hypertension (No=1, Yes=2).

Predictors or Concomitant variables

Concomitant variables for class determination: The concomitant variables include age, gender, education, marital status, and household wealth index.

Statistical Analysis

Latent Class Analysis is an innovative statistical method used to identify the latent classes of homogeneous individuals in a heterogeneous population [12]. The latent class was performed using the six indicators variables mentioned above. LCA uses observed dichotomous indicators to identify the unobserved latent class in a heterogeneous population. To determine the optimal number of latent class, we examined one to four model. The optimal number of latent classes was chosen based on the model having the smallest Akaike Information Criterion (AIC), Consistent Akaike Information Criterion (cAIC), Bayesian-Schwarz Information Criterion (BIC), adjusted Bayesian-Schwarz Information Criterion (aBIC), and Entropy [27,28]. A combination of parsimony and interpretability model selection criteria was used to carefully select the number of latent classes so that individuals are allocated to their most likely class. The output of the latent class analysis includes the number of latent classes, the latent class probability (i.e., the probability that an individual selected at random belonged to each latent class), and the conditional probability (i.e., the probability that an individual selector variable given that an individual belonged to a specific item of an observed indicator variable given that an individual belonged to a specific latent class).

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To determine the association between the concomitant variables (i.e., age, gender, education, marital status, and household wealth index) and the latent class, we apply the onestep technique approach. In this approach, the concomitant variables are included in the latent class regression model, and their coefficient is estimated simultaneously as part of the latent class model [29]. This approach has been proved to provide the best and unbiased coefficient estimates of the concomitant variables as compared to other methods [30]. Statistical analysis was conducted in R statistical software, and LCA was analyze using the poLCA package (Polytomous Variable Latent Class Analysis) [29].

Results

Descriptive Statistics

A total of 22,249 participants with chronic disease, i.e., diagnosed with diabetes or hypertension, were included in the analysis (Table 1). The participants in the age group 45-49 and 15-19 constitute the highest (21.31%) and the lowest (5.04%) percentage shares out of the total sample. Over half (51.17%) of the sample have completed secondary education, 24.6 percent were illiterate, and 79.56 percent were currently married. Further, among the chronic patients, the prevalence of smoking, consumption of alcohol, and aerated drinks were 4.17, 14.8, and 68.57 percent, respectively. Also, 81.13 percent of the participants reported suffering from hypertension, and 27.7 percent suffered from diabetes.

Background Characteristics	% (n=22,249)
Age	· · · · · · · · · · · · · · · · · · ·
15-19	5.04
20-24	8.38
25-29	12.17
30-34	14.96
35-39	19.19
40-44	18.95
45-49	21.31
Sex	
Male	13.88
Female	86.12
Education	
Illiterate	24.6
Primary	16.3
-	

 Table 1: Background characteristics of diabetes and hypertensive patients aged 15-49 years, NFHS-4, 2015-16.

Secondary	51.17
Higher Secondary	7.93
Marital Status	
Never married	13.57
Married	79.56
Widowed/Divorced/Separated	6.87
Wealth Index	
Poorest	16.72
Poorer	34.55
Middle	22.44
Richer	17.5
Richest	8.79
Observed Indicators	
Smoking	4.17
Drink alcohol	14.8
Take aerated drinks	68.57
Overweight or Obesity	43.26
Diabetes	27.7
Hypertension	81.13

Model fit and selection of Latent class

The model selection statistics for models are shown in Table 2. We fit the LCA models with classes ranging from 1 to 4. For each LCA model, the model fit indicators BIC, AIC, cAIC, and Entropy were calculated. According to the model fit indicators, a 3-Class model was selected as the best fit model as it has the lowest BIC, cAIC, and Entropy values. These three latent classes were labelled as "Diabetic with low-risk lifestyle", "High-risk lifestyle", and "Hypertensive with low-risk lifestyle". Figure 2 portrays the graphical representation of item response probability for the indicator's variables across the latent classes.

Table 2: Model fit statistics for the latent class models (n	=22,249)

No of classes	log- likelihood	Residual df	BIC	aBIC	cAIC	likelihood- ratio	Entrop y
1	-69173.11	57	138406. 3	138387. 2	138412. 3	17350.762	-
2	-61315.38	34	122921	122828. 9	122950	1859.196	1
3	-58920.21	11	118361	118195. 7	118413	1168.644	0.91
4	-59970.1	-12	120691	120452. 6	120766	2396.112	0.94

Latent class probability and the conditional probability of a "Yes" response for each indicator variables were summarized in Table 3. The last row in Table 3 indicates the

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probability of class membership in each latent class. About 21 percent of the participants were expected to belong to the Class 1 "diabetic with low-risk lifestyle", 8 percent to Class 2 "high-risk lifestyle", and 71 percent to Class 3 "hypertensive with low-risk lifestyle". Members in Class 1 were likely to report having high blood sugar level (diabetic) and likely to report not having smoked or drinking alcohol. Members in Class 2 are more likely to smoke and drink alcohol, and members in Class 3 are likely to report having high blood pressure and likely to report not having smoked or drink alcohol.

Figure 2: Item response conditional probability across the latent classes

 Table 3: The conditional probability of the response item and the latent class

 probability

Indicator Variables	Diabetic with low- risk lifestyle (Class 1)	High-risk lifestyle (Class 2)	Hypertensive with low- risk lifestyle (Class 3)
Smoking	0.04	0.55	0.02
Drink alcohol	0.12	0.81	0.14
Take aerated drinks	0.76	0.78	0.77
Overweight or Obesity	0.44	0.52	0.51
Diabetic	1.00	0.25	0.11
Hypertensive	0.00	0.88	1.00
Latent class probability	0.21	0.08	0.71

Covariates predicting latent class membership

Table 4 summarized the odds ratio (OR) from the latent regression model. Compared with respondents in the 15-19 years age group, those in the 20-29 age group were 4.1 times (OR=4.10) more likely to belong to class 2 (high-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Similarly, compared with respondents in the 15-19 years age group, those in the 45-49 age group were 1.7 times (OR=1.73) more likely to belong to class 3 (hypertensive with low-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Also, we observed that the odds of being in class 3 increases with the age of the respondents. With respect to males, females were less likely (OR=0.002) to belong to class 2 but more likely (OR=1.46) to belong to class 3. Higher odds of being in class 2-3 than to class 1 was observed among the married respondents (OR=1.54); however, widowed/divorced/separated were more likely to be in class 2 (OR=3.35), but less likely to be in class 3 (OR=0.98). Moreover, compared to the illiterate respondents, those with higher secondary education were less likely to belong to class 3 than

to class 1 (OR=0.79), and being in the richest quantile of wealth index lower the odds of being in class 3 than in class 1 (OR=0.69).

Peakersund Chanastaristics	Class 2 vs Class 1		Class 3 vs Class 1	
Background Characteristics	Odds Ratio	S.E	Odds Ratio	S. E
Age				
15-19	Ref		Ref	
20-24	4.10 ***	0.25	1.27 **	0.09
25-29	5.10 ***	0.25	1.34 ***	0.09
30-34	5.70 ***	0.26	1.42 ***	0.09
35-39	3.53 ***	0.26	1.42 ***	0.09
40-44	3.82 ***	0.27	1.51 ***	0.09
45-49	3.46 ***	0.27	1.73 ***	0.09
Gender				
Male	Ref		Ref	
Female	0.002 ***	0.34	1.46 ***	0.07
Education				
Illiterate	Ref		Ref	
Primary	1.03	0.19	0.73 ***	0.06
Secondary	1.08	0.17	0.79 ***	0.05
Higher Secondary	0.70	0.21	0.79 ***	0.08
Marital Status				
Never married	Ref		Ref	
Married	1.54 **	0.15	1.16 **	0.06
Widowed/Divorced/Separated	3.35 ***	0.35	0.98	0.08
Wealth Index				
Poorest	Ref		Ref	
Poorer	0.90	0.18	1.00	0.06
Middle	1.02	0.18	0.87 **	0.07
Richer	1.14	0.19	0.86 *	0.07
Richest	1.13	0.22	0.69 ***	0.08

Table 4: The latent classes of lifestyle behaviours and their associated covariates among
individuals aged 15-49 years

group: Class 1

Discussion

This study is the first in Northeast India that used latent class analysis to provides evidence about the pattern of modifiable risk factors among patients with diabetes or hypertension. Based on the response modifiable health risk behaviours, the LCA suggest three classes of respondents with diabetes or hypertension. These classes were characterized as "diabetic with low-risk lifestyle", "high-risk lifestyle", and "hypertensive with low-risk lifestyle".

More than 70 percent of the respondents belonged to the class "hypertensive with lowrisk lifestyle", which is they have their blood pressure level higher than normal and less likely

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to smoke. Several studies have acknowledged a significant elevation in blood pressure and an increase in the prevalence of hypertension following smoking cessation [31,32], which is possibly due to post-cessation weight gain [32]. Moreover, about 8 per cent of the respondents belonged to the class "high-risk lifestyle", mostly drink alcohol and smoke cigarette. This co-occurrence of alcohol use and cigarette smoking have been well documented in the existing studies [33,34]. In all the three identified classes, a vast majority of diabetic or hypertensive patients have a habit of consuming aerated drinks and have uncontrolled body weight. Studies suggest that sugar-sweetened beverages intake is the major contributor to weight gain and can increase the risk of T2 diabetes and hypertension [35,36]. Also, evidence from the study in Northeast India supports the positive correlation between overweight or obesity with diabetes and hypertension [16].

In line with the previous study [37], this study found that members aged 20 years and above are more likely to be in the high-risk cluster than the members below 20 years. Studies have explained that the teenage period is just the initial stage where an individual starts using or gets exposed to alcohol or smoking products. However, as this behaviour becomes a habit later, it may subsequently increase the intensity of substance use among older adults [38,39]. Also, it is well documented that starting to smoke and drink alcohol at an early age is associated with the number of cigarettes smoked and the quantity of alcohol consumed per day in adult age. According to Dawson, (2008) and Investigator, (1991), individuals who began to smoke or drink before the age of 20 years were most likely to consumed a large volume of alcohol and smoked more cigarettes per day as compared to those who started to smoke at the age of 20 or above [40,41]. Further, compared to young adults, older adults were more likely to report high blood pressure and less likely to smoke or drink alcohol. One reason could be the existing condition of high blood pressure; an older adult was most likely to have taken a precaution by lowering or quitting smoking and alcohol consumption to prevent further deterioration of health. Evidence from a recent study among older adults demonstrated that the main reason for smoking cessation attempt was the motivation towards better health [42]. It has been mentioned that hypertensive smokers were encouraged to quit smoking because of the risk of developing a severe form of hypertension such as malignant and renovascular hypertension [43]. Gender was found to be significantly associated with class 2 "high-risk lifestyle" and 3 "hypertensive with low-risk lifestyle". Consistent with the previous studies, in this study, female's respondents were less likely to be in the high-risk cluster than males' respondents [44]. One primary reason is that smoking and drinking alcohol by women is not socially and culturally

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accepted by many [45], and women are more concerned about their health and tend to avoid unhealthy lifestyle behaviour [46]. In our study, individuals from a wealthier household with a higher level of education were less likely to belong to a cluster of hypertensives with low substance use. An individual with higher education and better income can afford to pay for a healthier lifestyle, including regular physical exercise, accessibility to advanced and quality healthcare services; such efforts may reduce the risk of hypertension [47,48]. Being widowed/divorced/separated increased the likelihood of membership in the high-risk cluster. Studies about substance use by marital status have indicated that widowed or divorced individuals are most likely to consumed alcohol, cigarette, and marijuana as compared to singles [49,50].

To our knowledge, no study in India or Northeast India has study the clustering of health risk factor using the latent class approach. However, our study has some limitation. Firstly, the cross-sectional design of the study restricts us to measure the causal effect. Secondly, due to the dichotomous response on alcohol consumption, we cannot measure the quantity of alcohol an individual consumed.

Conclusions

This study identified three classes based on modifiable risk factors closely related to the risk of chronic disease. In addition, the study also identified factors that uniquely distinguished the identified classes. The intake of aerated drinks and obesity are the common modifiable risk factors in all three classes. As an initiative to healthy lifestyle behaviours, the findings suggest that males should control smoking and alcohol consumption, while females should control body weight and blood pressure. Further, we found that marital status and gender could be the preventive factors for high-risk smoking and alcohol drinking in Northeast India.

Contributors: Conceived and designed the research paper: SPM, HL. Analysed the data: SPM, HSC. Contributed agents/materials/analysis tools: SPM, HL, HSC. Wrote the manuscript: SPM, HSC. Refined the manuscript: SPM, HL, HSC.

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Patient consent for publication: Not applicable

Ethics approval: This study is based on the secondary data which is publicly available from the Demographic Health Survey website and the respondents are de-identified, hence ethical approval is not required for this study.

Data availability statement: Data were collected and owned by the Demographic Health Survey authority. Data are available at <u>https://dhsprogram.com/data/dataset/India_Standard-DHS_2015.cfm?flag=1</u> upon request.

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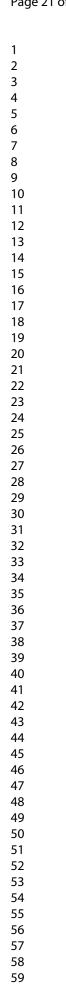
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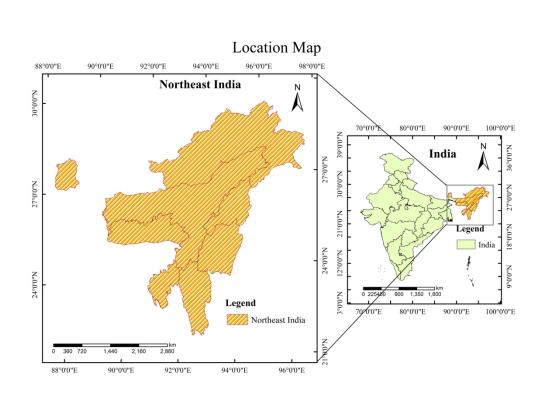
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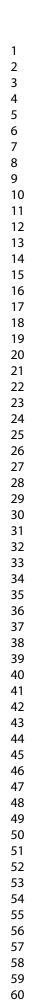
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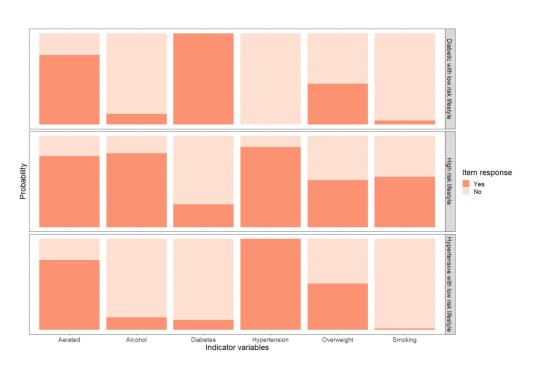




: Map showing the location of the Study area

190x131mm (300 x 300 DPI)





Item response conditional probability across the latent classes

129x84mm (300 x 300 DPI)

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Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods	•		
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	7
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	11
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Identifying the latent classes of modifiable risk behaviours among diabetic and hypertensive individuals in North Eastern India: a population-based cross-sectional study

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Identifying the latent classes of modifiable risk behaviours among diabetic and hypertensive individuals in North Eastern India: a population-based cross-sectional study

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MeSh Keywords:

Type 2 Diabetes ; Hypertension, Alcohol drinking, Smoking; Latent Class Analysis; North Eastern India.

Word Count: 4464

Abstract

Objective: To identify the latent classes of modifiable risk factors among the diabetic and hypertensive patients based on the observed indicators variables: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. We hypothesized that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Design: A cross-sectional study using a stratified random sampling method, and a nationally representative large-scale survey.

Setting and participants: The data come from the fourth round of the Indian National Family Health Survey, 2015-16. Respondents age 15-49 years who were diagnosed with either diabetes or hypertension, or both were included. The total sample is 22,249, out of which 3,284 were males, and 18,965 females.

Primary and secondary outcome measures: The observed variables used as latent indicators are: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. The concomitant variables include age, gender, education, marital status, and household wealth index. Latent class model was used to simultaneously identify the latent class and to determine the association between the concomitant variables and the latent classes.

Results: Three latent classes were identified and labelled as Class 1: "Diabetic with low-risk lifestyle" (21%), Class 2: "High-risk lifestyle" (8%), and Class 3: "Hypertensive with low-risk lifestyle" (71%). Class 1 is characterised by those with a high probability of having diabetes and low probability of smoking and drinking alcohol. Class 2 characterized by a high probability of smoking and drinking alcohol. Class 3 by a high probability of having high blood pressure and low probability of smoking and drinking and drinking alcohol.

Conclusions: Males should control smoking and alcohol consumption, while females should control their body weight and blood pressure. Policy and intervention programmes in Norteastern India should focus on targeting multiple modifiable risk behaviours that are most likely to co-occur within an individual.

Keywords: Modifiable risk; Diabetes; Hypertension; Latent class analysis; Northeastern India.

Strengths and limitations of the study

- The sample for the study is relatively large as it uses a nationally representative largescale data.
- Respondents' status of diabetes and hypertension is as diagnosed during fieldwork (on the day of interview) using a standard biomarker instrument and measurement.
- Latent class analysis (LCA) is a person-centred technique and the appropriate method for explaining the clustering of health risk behaviours.
- > The cross-sectional design of the study restricts us to measure the causal effect.
- Modifiable risk factors were collected based on dichotomous responses, which limits measuring the intensity of substance use.

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Introduction

Effective lifestyle modification plans and affordable approaches to control high blood sugar and high blood pressure level benefit the at-risk population [1,2]. The leading causes of mortality due to chronic diseases in adults, particularly older adults, are linked to unhealthy lifestyle and behaviours [3], such as tobacco consumption, physical inactivity, excess alcohol consumption, and poor diet. An alarmingly high prevalence of hypertension in North Eastern (NE) India has been reported in recent studies [4-6]. Sikkim has the highest prevalence of hypertension among all the Indian states, while other NE states such as Nagaland, Assam, Arunachal Pradesh, Mizoram, and Tripura have prevalence above 11.0 percent, which is well above the national average [5,6]. Further, according to the Global Burden of Disease (GBD) study, the percentage change of diabetes prevalence between 1990 and 2016 has increased by more than 20 percent across the states of Northeastern India [7]. This percentage change was highest in the states of Sikkim, Arunachal Pradesh, and Nagaland.

Modifiable health risk behaviours such as smoking, heavy consumption of alcohol, low physical activity, and unhealthy diet characterized by high intake of sugar and fats, low consumption of fruits and vegetables are the major causes of non-communicable diseases (NCDs) [8], and strongly linked with early mortality [9,10]. Usually, these risk behaviours exist simultaneously or cluster within individuals [11]. It is argued that lifestyle risk factors within individuals are not random, but more likely to cluster with other unhealthy behaviours [12,13]. Further, when two risk behaviours cluster together with each other more than the other factors, it may suggests that they could be influenced by a common source [14]. Moreover, modifiable risk behaviours for chronic diseases such as excessive use of alcohol, cigarette smoking, obesity and unhealthy diets are unlikely to occur in an entirely uniform manner in a population. That is, it is uncertain whether people can be accurately classify into two groups, as those adapting to a healthy versus those unhealthy lifestyle. For example, certain individuals who engage in more vigorous physical activities tend to consume alcohol more frequently than their inactive counterparts [15]. Also, cigarette smoking is associated with lower rate of obesity among certain individuals [16]. In a study among the US adults, Leventhal et al. (2014) used modifiable risk factors like usage of alcohol, drug, nicotine, current obesity status, and weekly physical activity and found that the adult population clusters into five sub-groups based on the pattern of these modifiable risk factors [14]. Another study in India by Shaikh and Khan (2021),

found that hypertension is more likely to cluster with other modifiable risk behaviours such as smoking, alcohol, chewing tobacco, obesity, and unhealthy diets in both men and women [17]. Atorkey and Owiredua (2021), in their study that identified the clustering of five multiple health risk behaviours, also found that low vegetable and fruit intake, and low physical activity cluster together within an individual, whereas smoking tobacco and alcohol consumption co-occur together forming another cluster [18]. The pattern of clustering of modifiable risk behaviours could also differ by region and community level, as evident from previous studies [17,19]. The clustering of two or more modifiable risk behaviours is of great concern because it can intensify the risk of developing chronic diseases and cardiovascular mortality [20,21], and most intervention measures are specific to a single risk factors. For example, in Asia 43.5 percent of Chinese adults and 37 percent of Korean adults had at least two cardiovascular risk factors [11,22]. Moreover, in India, 35.6 percent of adult men and 10 percent adult women have at least three lifestyle risk factors [17]. It is also found that a combination of smoking and heavy drinking emerged as the riskiest behaviour for all causes of death [23].

The majority of studies reported a higher prevalence of smoking, excess alcohol consumption, physical inactivity, and poor diet among people with diabetes or hypertension than those without diabetes or hypertension [24,25]. Notably, previous studies have examined diabetic or hypertensive patients as a single homogeneous group without considering the possible heterogeneity existing within the population [26]. Most of the existing studies on health risk behaviours have emphasized only changing a single unhealthy behaviour [25,27]. However, interventions that simultaneously target these unhealthy behaviours are necessary from the policy perspective [11].

Existing studies in India on clustering of NCDs risk factors have used intraclass correlation and scoring methods [17,19,28]. However, studies have suggested that LCA is the most appropriate method for explaining the clustering of health risk behaviours [29,30]. LCA is a probabilistic model approach designed for identifying clusters based on dichotomous variables. This study is also an attempt to explore the clustering of NCD risk factors using the LCA approach in Northeastern India. The aims is to identify the latent classes of modifiable risk factors among diabetic and hypertensive patients based on the observed indicator variables such as smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. We applied LCA, also to investigate heterogeneity in the population of an individual with diabetes and hypertension based on the responses of observed risk factors. More specifically, the objective is to describe how individuals in Northeast India diagnosed with diabetes or

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hypertension are clustered according to the pattern of observed risk factors and identify the difference between these groups based on socio-demographic characteristics. Information on clustering of health risk behaviours become vital as it guides in designing the disease control programs. Intervention approach that aimed at targeting multiple modifiable risk behaviours in a single program are gaining importance because they are potentially most cost-effective, efficient and may have a great public health impact than the single modifiable risk approaches. Therefore, we hypothesize that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Methods

Study location

The study focuses on the Northeastern region (NER) of India comprising eight states, namely Assam, Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, and Tripura (Figure 1). Most parts of the region has a hilly terrain and inhabited mainly by myriad tribes belonging to different cultures and ethnic communities [31]. The region has over 45 million population, which is 3.8 percent of India's population, with a density of 159 persons per km² [32].

Design and Setting

The NFHS-4 (2015-16), a nationally representative large scale survey, is a cross-sectional study that adopted a stratified two-stage random sampling design for both urban and rural areas, including a systematic mapping and listing of households in the selected primary sampling units (PSUs). The analysis is based on the publicly available data, in which the identity of selected respondents, households, and geocodes of PSUs are concealed [33]. In the first stage, the PSUs were selected based on probability proportional to population size (PPS). Rural PSUs are the villages, while census enumeration blocks (CEBs) formed the PSUs in urban areas. In the second stage, systematic random sampling was done in each PSUs to select households for the sample. At the household level, information were sought from the heads, eligible women age 15 - 49 years, and men age 15 - 54 years, alongwith their biomarkers and blood samples on a specially designed Dried Blood Spots (DBS). A detailed description of the survey design can be found elsewhere [33].

The data used in this study is the fourth round of the Indian National Family Health Survey (NFHS-4) conducted during 2015-16. The data was downloaded from the DHS website [34]. The NFHS series of surveys has been initiated by the Ministry of Health and Family Welfare, Government of India, and coordinated by the International Institute for Population Sciences, Mumbai.

Sample

The study includes only individuals age 15-49 years who were diagnosed with either diabetes or hypertension, or both. The total sample size is 22,249, of which 3,284 were males, and 18,965 were females for the Northeastern region of India.

Patient and Public Invlovement

No patient involved

Measures

Diabetes: Fingerstick blood is collected, and blood glucose level is determined using the FreeStyle Optium H Glucometer. A respondent is considered diagnosed with diabetes if the random blood sugar level is >140mg/dl [33].

Hypertension: Blood pressure (BP) level was measured using an OMRON Blood Pressure measuring device. Three separate blood pressure readings were taken with an interval of 5 minutes between readings. A respondent is considered hypertensive if the systolic blood pressure is \geq 140 mmHg, or diastolic blood pressure \geq 90 mmHg, or if the respondent was taking antihypertensive medication to lower blood pressure at the time of the survey [33].

Overweight or obesity: In this study, we categorized continuous body mass index (BMI) according to the WHO guidelines for the Asian population. A respondent is classified as overweight or obese if BMI is $\geq 23 \text{ kg/m}^2$ [35].

Outcome Variables of Interest

Observed Indicator variables: The observed variables used as latent indicators are cigarette smoking (No=1, Yes=2), Alcohol consumption (No=1, Yes=2), Takes aerated drink (No=1, Yes=2), Overweight or obesity (No=1, Yes=2), Diabetes (No=1, Yes=2), and Hypertension (No=1, Yes=2).

Predictors or Concomitant variables

Concomitant variables for class determination: The concomitant variables include age, gender, education, marital status, and household wealth index.

Statistical Analysis

Latent Class Analysis (LCA), based on structural equation modelling, is a personcentred analytical approach that allows the identification of homogeneous sub-groups in a heterogeneous population. LCA is similar to cluster analysis because individuals are classifying into homogenous unobserved (latent) groups based on the response pattern to a set of observed variables. However, in cluster analysis, objects are classified based on distance measures, whereas in LCA classification are based on probabilistic and finite mixture modelling approach [36,37]. A latent class model splits the population into mutually exclusive and exhaustive groups that are homogeneous within the groups but differ among them. Several studies have adopted the LCA approach to identify risk factors clustering within the heterogeneous population. In a study by Dey et al (2016), based on seven observed risk factors, LCA was used to classify individuals into two latent class "susceptible to adverse health outcomes groups" and "not susceptible to adverse health outcomes groups" [38]. Another study in China applied LCA to ten observed complications and comorbidities of T2 diabetic patients and categorized the individuals into four latent classes, namely "complications and comorbidity groups", "high risk of complications group", "high risk of comorbidities and Cardio Vascular Disease groups", and "diabetes without complications and comorbidities group" [39]. A study in West Azerbaijan province among the hypertensive patients aged 50 years and above used four indicators such as dietary patterns, physical activity, tobacco use, and high blood pressure control to categorized the hypertensive patients into three latent classes [40].

Latent Class Analysis is an innovative statistical method used to identify the latent classes of homogeneous individuals in a heterogeneous population [39]. The latent class was performed using the six indicators variables mentioned above. LCA uses observed dichotomous indicators to identify the unobserved latent class in a heterogeneous population. To determine the optimal number of latent classes, we examined one to four models. The optimal number of latent classes was chosen based on the model having the smallest Akaike Information Criterion (AIC), Consistent Akaike Information Criterion (CAIC), Bayesian-Schwarz Information Criterion (BIC), adjusted Bayesian-Schwarz Information Criterion

(aBIC), and Entropy [41,42]. A combination of parsimony and interpretability model selection criteria was used to carefully select the number of latent classes so that individuals are allocated to their most likely class. The outputs of the latent class analysis includes the number of latent classes, the latent class probability (i.e., the probability that an individual selected at random belonged to each latent class), and the conditional probability (i.e., the probability that an individual would give a particular response to a specific item of an observed indicator variable given that an individual belongs to a specific latent class).

To determine the association between the concomitant variables (i.e., age, gender, education, marital status, and household wealth index) and the latent class, we apply the onestep technique approach. In this approach, the concomitant variables are included in the latent class regression model, and their coefficient is estimated simultaneously as part of the latent class model [43]. This approach has been demonstrated to provide the best and unbiased coefficient estimates of the concomitant variables as compared to other methods [44]. Statistical analysis was conducted in R statistical software, and LCA was analyze using the poLCA package (Polytomous Variable Latent Class Analysis) [43].

Figure 2: Conceptual framework of the study. Source: Authors

Results

Descriptive statistics

A total of 22,249 individuals with chronic diseases, i.e., diagnosed with diabetes or hypertension, were included in the analysis (Table 1). Individuals in the age group 45-49 and 15-19 constitute the largest (21.3%) and the lowest (5.0%) respectively in the total sample. Over half (51.2%) of the sample have completed secondary education, 24.6 percent were illiterate, and 79.6 percent were currently married. Further, among the chronic disease patients, the prevalence of smoking, consumption of alcohol, and aerated drinks were 4.2, 14.8, and 68.6 percent respectively. Also, 81.1 percent of the participants reported suffering from hypertension, and 27.7 percent from diabetes. The sample distribution also indicates that chronic condition is much higher among females (86.1%) than males (13.9%), among older ages (age 35+), and among poorer households.

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Table 1: Percent distribution of adults of age 15-49 years with chronic condition
(diabetic and hypertensive patients) by selected background characteristics,
Northeastern India, NFHS-4, 2015-16.

Background Characteristics	% (n=22,249)
Age	
15-19	5.04
20-24	8.38
25-29	12.17
30-34	14.96
35-39	19.19
40-44	18.95
45-49	21.31
Sex	
Male	13.88
Female	86.12
Education	
Illiterate	24.6
Primary	16.3
Secondary	51.17
Higher Secondary	7.93
Marital Status	
Never married	13.57
Married	79.56
Widowed/Divorced/Separated	6.87
Wealth Index	
Poorest	16.72
Poorer	34.55
Middle	22.44
Richer	17.5
Richest	8.79
Observed Indicators	
Smoking	4.17
Drink alcohol	14.8
Take aerated drinks	68.57
Overweight or Obesity	43.26
Diabetes	27.7
Hypertension	81.13

Model fit and selection of Latent class

The model fit/selection statistics to derive appropriate models are shown in Table 2. We fit the LCA models with classes ranging from 1 to 4. For each LCA model, the model fit indicators BIC, AIC, cAIC, and Entropy were calculated. According to the model fit indicators, a three-Class model has been selected as the best fit model as it has the lowest BIC and cAIC values. Smaller values on each indicator suggest a better model, or a model with few explanatory variables or parameters, and inform the decision of the best model to be retained [45]. Another diagnostic indicator is entropy [46], which indicates how accurately the model defines the

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classes. In general, an entropy value close to 1.0 is considered as ideal [47], and above 0.8 is also acceptable. An entropy value of 1.0 would indicate that every individual has been perfectly classified within the classes based on the responses of the observed indicators. The three latent classes were labelled as "Diabetic with low-risk lifestyle", "High-risk lifestyle", and "Hypertensive with low-risk lifestyle". Figure 3 portrays the graphical representation of item response probability for the indicator's variables across the latent classes.

No of classes	log-likelihood	Residual df	BIC	aBIC	cAIC	likelihood-ratio	Entropy
1	-69173.11	57	138406.3	138387.2	138412.3	17350.762	-
2	-61315.38	34	122921	122828.9	122950	1859.196	1.0
3	-58920.21	11	118361	118195.7	118413	1168.644	0.91
4	-59970.1	-12	120691	120452.6	120766	2396.112	0.94

 Table 2: Model fit statistics for the latent class models (n=22,249)

Latent class probability and the conditional probability of a "Yes" response for each indicator variables were summarized in Table 3. The last row in Table 3 indicates the probability of class membership in each latent class. About 21 percent of the participants were expected to belong to the Class 1 "diabetic with low-risk lifestyle", 8 percent to Class 2 "high-risk lifestyle", and 71 percent to Class 3 "hypertensive with low-risk lifestyle". Members in Class 1 were likely to report having high blood sugar level (diabetic) and unlikely to smoke cigarette and drink alcohol, and members in Class 3 are likely to report having high blood pressure and unlikely to smoke cigarette or drink alcohol.

Figure 3: Item response conditional probability across the latent classes. Source: Authors

Indicator Variables	Diabetic with low- risk lifestyle (Class	High-risk lifestyle (Class 2)	Hypertensive with low- risk lifestyle (Class 3)
	1)	· · · · ·	* ` ` `
Smoking	0.04	0.55	0.02
Drink alcohol	0.12	0.81	0.14
Take aerated drinks	0.76	0.78	0.77
Overweight or Obesity	0.44	0.52	0.51
Diabetic	1.00	0.25	0.11
Hypertensive	0.00	0.88	1.00
Latent class probability	0.21	0.08	0.71

Table 3: The conditional probability of the response items and the latent classprobability for study sample in Northeastern India, NFHS-4, 2015-16

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Table 4 presents the distribution of socio-economic and demographic characteristics of the individuals by the three latent classes. Age, gender, education, marital status, and household wealth index were statistically found significantly associated with the three latent classes at 1 percent level of significant. The hypertensive with low-risk lifestyle class has the highest proportion of respondents aged 45-49 years, whereas both diabetic with low-risk lifestyle class and high-risk lifestyle class has the highest proportion of respondents aged 35-39 years (19.4%) and 19.5% respectively). Both the diabetic with low-risk lifestyle class (10.6% males vs. 89.4% females) and the hypertensive with low-risk lifestyle class (6.2% males vs. 93.8% females) has the highest proportion of females; males constituted almost 100 percent of the high-risk lifestyle class (99.2% males vs. 0.8% females). Lower proportion of the respondents have completed higher secondary education in case of both diabetic with low-risk lifestyle class (10.5%) and hypertensive with low-risk lifestyle class (8.5%). Marital status shows a similar pattern in all the three classes; higher proportion of married respondents and lower proportion of widowed/divorced/separated respondents (<10%). The Wealth index shows that respondents belonging to the middle quintile constituted the largest proportion in the diabetic with low-risk lifestyle class (27.2%), and high-risk lifestyle class (26.6%). However, respondents belonging to the poorer wealth quintile have the highest proportion of hypertensive with low-risk lifestyle class (29.4%).

Background Characteristics	"Diabetic with low- risk lifestyle" class (n=4727, 21%)	"High-risk lifestyle" class (n=1828, 8%)	"Hypertensive with low-risk lifestyle" class (n=15,694, 71%)	P-value ^a
Age	· · ·			< 0.01
15-19	8.08	3.06	4.96	
20-24	8.99	8.37	7.6	
25-29	12.88	13.51	11.93	
30-34	15.30	18.00	15.29	
35-39	19.40	19.53	19.46	
40-44	17.73	19.09	19.04	
45-49	17.62	18.44	21.72	
Gender				< 0.01
Male	10.62	99.18	6.17	
Female	89.38	0.82	93.83	
Education				< 0.01
Illiterate	17.96	11.65	25.17	
Primary	16.50	15.10	15.85	
Secondary	55.05	58.70	50.50	
Higher Secondary	10.49	14.55	8.47	
Marital Status				< 0.01
Never married	19.93	21.55	14.30	

Table 4: Percent distribution of diabetic and hypertensive patients age 15-49 years according to three latent classes by background characteristics, Northeastern India, NFHS-4, 2015-16

Married	72.75	75.22	78.41	
Widowed/Divorced/Se parated	7.32	3.23	7.30	
Wealth Index				< 0.01
Poorest	10.94	12.14	12.94	
Poorer	26.06	24.84	29.43	
Middle	27.23	26.64	26.30	
Richer	22.49	23.34	21.25	
Richest	13.29	12.04	10.07	
Total	100.0	100.0	100.0	

Note: ^aBased on chi-squared tests of association.

Covariates predicting latent class membership

Table 5 summarized the odds ratios (OR) results from the latent regression model. Compared with respondents in the 15-19 years age group, those in the 20-29 age group were 4.1 times (OR=4.10; p-<0.01) more likely to belong to class 2 (high-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Similarly, compared with respondents in the 15-19 years age group, those in the 45-49 age group were 1.7 times (OR=1.73; p-<0.01) more likely to belong to class 3 (hypertensive with low-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Also, we observed that the odds of being in class 3 increases with the age of the respondents. With respect to males, females were less likely (OR=0.002; p-<0.01) to belong to class 2 but more likely (OR=1.46; p-<0.01) to belong to class 3. Higher odds of being in class 2-3 than to class 1 was observed among the married respondents (OR=1.54). Similarly, widowed/divorced/separated were more likely to be in class 2 (OR=3.35; p-<0.01), but less likely to be in class 3 (OR=0.98; p-<0.01). Moreover, compared to the illiterate respondents, those with higher secondary education were less likely to belong to class 3 than to class 1 (OR=0.79; p-<0.01), and being in the richest wealth quintile lower is the odds of being in class 3 than in class 1 (OR=0.69; p-<0.01).

Table 5: The odds for various latent classes of lifestyle behaviours and their associated covariates among individuals age 15-49 years, Northeastern India, NFHS-4, 2015-16

Background Characteristics	Class 2 vs Class 1		Class 3 vs Class 1	
Background Characteristics	Odds Ratio	S. E	Odds Ratio	S. E
Age				
15-19	Ref		Ref	
20-24	4.10 ***	0.25	1.27 **	0.09
25-29	5.10 ***	0.25	1.34 ***	0.09
30-34	5.70 ***	0.26	1.42 ***	0.09
35-39	3.53 ***	0.26	1.42 ***	0.09
40-44	3.82 ***	0.27	1.51 ***	0.09
45-49	3.46 ***	0.27	1.73 ***	0.09

Gender				
Male	Ref		Ref	
Female	0.002 ***	0.34	1.46 ***	0.07
Education				
Illiterate	Ref		Ref	
Primary	1.03	0.19	0.73 ***	0.06
Secondary	1.08	0.17	0.79 ***	0.05
Higher Secondary	0.70	0.21	0.79 ***	0.08
Marital Status				
Never married	Ref		Ref	
Married	1.54 **	0.15	1.16 **	0.06
Widowed/Divorced/Separated	3.35 ***	0.35	0.98	0.08
Wealth Index				
Poorest	Ref		Ref	
Poorer	0.90	0.18	1.00	0.06
Middle	1.02	0.18	0.87 **	0.07
Richer	1.14	0.19	0.86 *	0.07
Richest	1.13	0.22	0.69 ***	0.08

Ref: Reference group; ***p-value<0.01; **p-value<0.05; *p-value<0.1; S.E: Standard Error; Reference group: Class 1

Discussion

This study is the first attempt in Northeastern India, a region characterized by a seemingly homogenous racial group but inhabited by ethno-lingually diverse sub-populations, that applied latent class analysis to provide evidence about the pattern of modifiable risk factors among people suffering from diabetes or hypertension. Based on the observed modifiable health risk behaviours, the LCA suggests presence of three classes of respondents with diabetes or hypertension: "diabetic with low-risk lifestyle", "high-risk lifestyle", and "hypertensive with low-risk lifestyle". The findings portray that the 22,249 odd diabetic or hypertensive persons in the region can be categorized into three groups or classes, with homogeneity in their characteristics within the group but heterogeneous between the groups. One of the three latent classes has a 100 percent likelihood of having one of the risk factors combined with a low and moderate probability of having the other five risk factors. Each of the classes exhibit a unique risk factor configurations, and socio-economic and demographic profiles from one another. Thus, chronic diseases prevention programmes that specially target and reach out to the at-risk sub-populations will be beneficial and effective, as illustrated in this analysis (Table 3 and 5).

More than 70 percent of the respondents belong to the class "hypertensive with lowrisk lifestyle" have their blood pressure level higher than normal and less likely to smoke and use alcohol. Evidence from a large body of existing literature supports that cigarette smoking leads to an immediate increase in blood pressure level and heart rate [48]. The effect of cigarette smoking on blood pressure and heart rate is largely due to the nicotine content in the cigarrettes [48]. However, studies also found a significant elevation in blood pressure and an increase in the prevalence of hypertension following smoking cessation [49,50], which could possibly be due to post-cessation weight gain [48,49]. Green et al. (1986) had concluded that smoking cessation in itself is not likely to result in a lowering blood pressure but on the contrary it may result even in higher blood pressure [51]. Moreover, about 8 percent of the respondents belonging to the "high-risk lifestyle" class mostly drink alcohol and smoke cigarettes. This cooccurrence of alcohol use and cigarette smoking have been well documented in the existing studies [52,53], and evidence suggest that a common genetic trait play a role in the cooccurance of smoking and alcohol use [54,55]. Epidemiological studies have also shown that individuals who are dependent on nicotine are more than four time more likely to be dependent on alcohol. Similarly, individuals who are dependent on alcohol are also more than three times more likely to be dependent on nicotine with reference to the general population [56]. Stress is another factor that influences use of tobacco and alcohol. For example, people who drink alcohol are most likely to smoke in an attempt to overcome stress [57]. Literature also suggest cross tolerance effect between alcohol and tobacco. It is found that the stimulating effect of nicotine in tobacco is restrained by the sedating effect of alcohol, which entices smokers to drink more alcohol [58]. Alcohol's sedating effect reduces the physiological effect of nicotine, thus increasing the consumption of tobacco.

In all the three identified classes, a vast majority of diabetic or hypertensive persons appear to have a habit of consuming aerated drinks and an uncontrolled body weight. Studies suggest that sugar-sweetened beverages intake is the major contributor to weight gain and can increase the risk of T2 diabetes and hypertension [59,60]. Cross-sectional studies acknowledge the positive association between overweight and obesity with the consumption of aerated drinks or sugar-sweetened beverages. For example, studies infer that women who consumed sweetened beverages more than once a week were more likely to be overweight than those who consumed sweetened beverages less than once a week [61]. Other studies found that women who consumed sugar-sweetened beverages regularly were heavier by 0.2 kg than the non-consumers [62]. The intake of sodas sweetened with high-fructose corn syrup is associated with hypertension among adolescents population [63]. Also, a spurt in the prevalence of hypertension have been observed among individuals who consumed more than average amount of fructose [64]. Evidence from a cross-sectional study in Northeast India supports the positive correlation between overweight or obesity with diabetes and hypertension [26]. The plausible

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explanation is that both sugar sweetened beverages and artificial sweetened beverages are associated with the development of metabolic derangements that in turn might lead to elevated blood pressure [65]. High intake of sugar-sweetened beverages contributes to a higher total energy consumption, which increases energy intake without an increase in energy expenditure certainly results in weight gain. There is no dearth of scientific evidence which support the notion that decreasing aerated drinks consumption reduces the prevalence of overweight and obesity.

As observed in a previous study [66], this study also found that those aged 20 years and above are more likely to be in the 'high-risk cluster' than those below 20 years. Studies have elucidated that the adolescence or teenage stage is just the initial stage when an individual starts using or exposed to alcohol or tobacco (smoking) products. However, as this behaviour becomes a habit later on, it subsequently accentuates the intensity of substance (ab)use among older adults [67,68]. Also, it is well documented that initiation of smoking and drinking alcohol at an early age is associated with the number of cigarettes smoked and the quantity of alcohol consumed per day in adult age. According to Investigator (1991) and Dawson et al. (2008), individuals who began to smoke or drink before the age of 20 years were most likely to consumed a large volume of alcohol and smoked more cigarettes per day as compared to those who started after the age of 20 or above [69,70]. Further, compared to young adults, older adults were more likely to report high blood pressure and less likely to smoke or drink alcohol. One reason could be the existing condition of high blood pressure; an older adult was most likely to have taken a precaution by lowering or quitting smoking and alcohol consumption to prevent further deterioration of health. Evidence from a recent study among older adults demonstrated that the main reason for smoking cessation attempt was the motivation towards better health [71]. Hypertensive smokers were encouraged to quit smoking because of the risk of developing a severe form of hypertension such as malignant and renovascular hypertension [72]. Gender factors are also found to be significantly associated with class 2 "high-risk lifestyle" and 3 "hypertensive with low-risk lifestyle". Consistent with the previous studies, in this study also, female respondents were less likely to be in the high-risk cluster than males [73]. One primary reason stated is that smoking and drinking alcohol by women is not socially and culturally accepted by many [74], and women are more concerned about their health and tend to avoid unhealthy lifestyle behaviours [75]. In our study, individuals from a wealthier households with higher education were less likely to belong to a cluster of hypertensive with low substance use. An individual with higher education and better income can afford to pay for

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a healthier lifestyle, including regular physical exercise, accessibility to advanced and quality healthcare services, as such efforts may reduce the risk of hypertension [76,77]. Being widowed/divorced/separated tend to increase the likelihood of falling into the high-risk cluster. Substance use by marital status indicated that widowed or divorced individuals are most likely to consumed alcohol, cigarette, and marijuana as compared to singles [78,79].

A search of similar studies indicates that no study in India or Northeast India has examined the clustering of health risk factors using the latent class approach. However, our study has some limitations. Firstly, the cross-sectional design of the study restricts us to measure the causal effect. Second, due to the dichotomous response on alcohol consumption, we cannot measure the quantity of alcohol an individual consumed.

Conclusion

In Northeastern India, as this study illustrates, there are three classes of modifiable risk factors closely related to the risk of chronic diseases (diabetes and hypertension). In addition, the study also identified factors that uniquely distinguished the identified classes. The intake of aerated drinks and obesity are the common modifiable risk factors in all three classes. As an initiative to healthy lifestyle behaviours, the findings suggest that males should control smoking and alcohol consumption, while females should control body weight and blood pressure. Further, we found that marital status and gender could be the catalyst to prevent high-risk smoking and alcohol drinking in Northeastern India. Also, the study observes smoking and alcohol use are the two modifiable risk behaviours, which tends to co-occur within an individual. Therefore, it is recommended that policy and intervention programmes in Norteastern India that promote healthy lifestyles should focus on targeting multiple modifiable risk behaviours that are most likely to co-occur within an individual. On the other hand, awareness about adapting to healthy diets and weight control along with physical exercises should be promoted with rigour in the region.

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Data availability statement: Data stored and maintained by the Demographic Health Survey office, and available to public at <u>https://dhsprogram.com/data/dataset/India_Standard-DHS_2015.cfm?flag=1</u> upon request.

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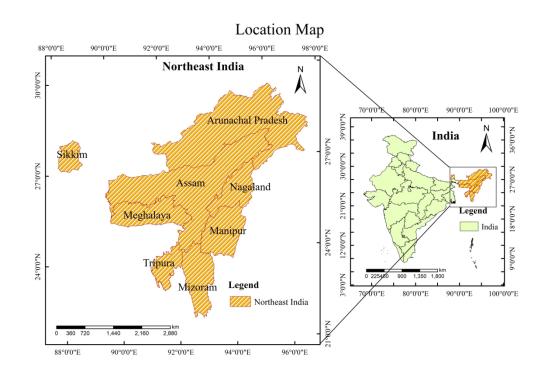
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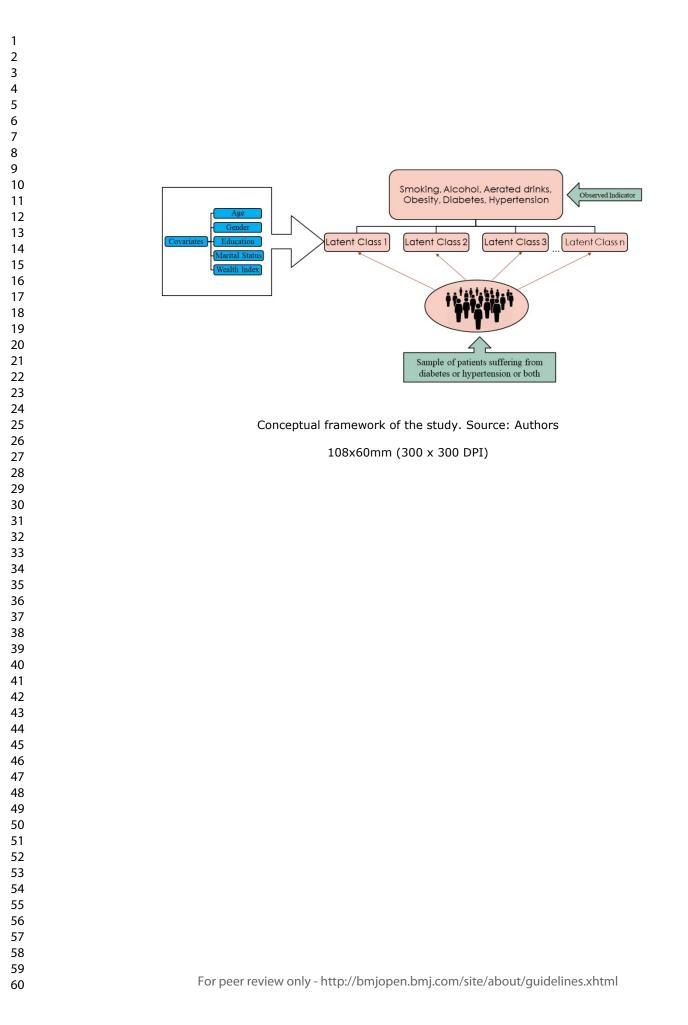
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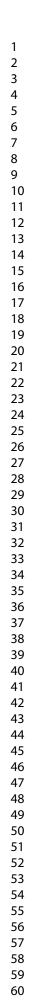


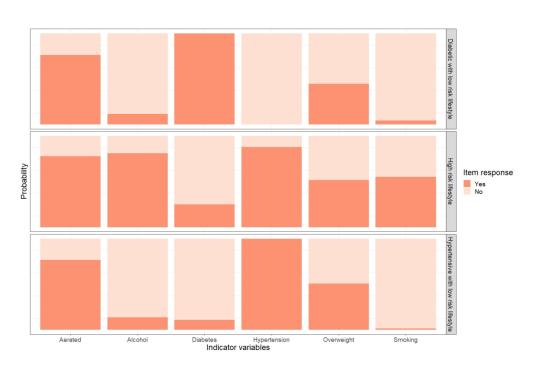
Map showing the location of the Study area. Source: Authors

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Item response conditional probability across the latent classes. Source: Authors

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Section/Topic	ltem #	Recommendation	Reported on page #			
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1			
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1			
Introduction						
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4			
Objectives	3	State specific objectives, including any prespecified hypotheses	4			
Methods						
Study design	4	Present key elements of study design early in the paper	5			
Setting						
articipants 6 (a) Give the eligibility criteria, and the sources and methods of selection of participants						
Variables	ariables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable					
Data sources/						
measurement		comparability of assessment methods if there is more than one group				
Bias	9	Describe any efforts to address potential sources of bias				
Study size	10	Explain how the study size was arrived at	5			
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why				
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6			
		(b) Describe any methods used to examine subgroups and interactions				
		(c) Explain how missing data were addressed				
		(d) If applicable, describe analytical methods taking account of sampling strategy				
		(e) Describe any sensitivity analyses				

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	7
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		10	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	11
		which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Identifying the latent classes of modifiable risk behaviours among diabetic and hypertensive individuals in North Eastern India: a population-based cross-sectional study

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Identifying the latent classes of modifiable risk behaviours among diabetic and hypertensive individuals in North Eastern India: a population-based cross-sectional study

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MeSh Keywords:

Type 2 Diabetes; Hypertension, Alcohol drinking, Smoking; Latent Class Analysis; North Eastern India.

Word Count: 4464

Abstract

Objective: To identify the latent classes of modifiable risk factors among the diabetic and hypertensive patients based on the observed indicators variables: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. We hypothesized that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Design: A cross-sectional study using a stratified random sampling method, and a nationally representative large-scale survey.

Setting and participants: Data come from the fourth round of the Indian National Family Health Survey, 2015-16. Respondents aged 15-49 years who were diagnosed with either diabetes or hypertension or both were included. The total sample is 22,249, out of which 3,284 were males, and 18,965 were females.

Primary and secondary outcome measures: The observed variables used as latent indicators are: smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. The concomitant variables include age, gender, education, marital status, and household wealth index. Latent class model was used to simultaneously identify the latent class and to determine the association between the concomitant variables and the latent classes.

Results: Three latent classes were identified and labelled as Class 1: "Diabetic with low-risk lifestyle" (21%), Class 2: "High-risk lifestyle" (8%), and Class 3: "Hypertensive with low-risk lifestyle" (71%). Class 1 is characterised by those with a high probability of having diabetes and low probability of smoking and drinking alcohol. Class 2 characterized by a high probability of smoking and drinking alcohol. Class 3 by a high probability of having high blood pressure and low probability of smoking and drinking and drinking alcohol.

Conclusions: Co-occurrence of smoking and alcohol consumption were prevalent in men, while excess body weight and high blood pressure were prevalent in women. Policy and programmes in Northeastern India should focus on targeting multiple modifiable risk behaviours that co-occur within an individual.

Keywords: Modifiable risk; Diabetes; Hypertension; Latent class analysis; Northeastern India.

Strengths and limitations of the study

- The sample for the study is relatively large as it uses a nationally representative largescale data.
- Respondents' status of diabetes and hypertension is as diagnosed during fieldwork (on the day of interview) using a standard biomarker instrument and measurement.
- Latent class analysis (LCA) is a person-centred technique and the appropriate method for explaining the clustering of health risk behaviours.
- > The cross-sectional design of the study restricts us to measure the causal effect.
- Modifiable risk factors were collected based on dichotomous responses, which limits measuring the intensity of substance use.

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Introduction

Effective lifestyle modification plans and affordable approaches to control high blood sugar and high blood pressure level benefit the at-risk population [1,2]. The leading causes of mortality due to chronic diseases in adults, particularly older adults, are linked to unhealthy lifestyle and behaviours [3], such as tobacco consumption, physical inactivity, excess alcohol consumption, and poor diet. An alarmingly high prevalence of hypertension in North Eastern (NE) India has been reported in recent studies [4-6]. Sikkim has the highest prevalence of hypertension among all the Indian states, while other NE states such as Nagaland, Assam, Arunachal Pradesh, Mizoram, and Tripura have prevalence above 11.0 percent, which is well above the national average [5,6]. Further, according to the Global Burden of Disease (GBD) study, the percentage change of diabetes prevalence between 1990 and 2016 has increased by more than 20 percent across the states of Northeastern India [7]. This percentage change was highest in the states of Sikkim, Arunachal Pradesh, and Nagaland.

Modifiable health risk behaviours such as smoking, heavy consumption of alcohol, low physical activity, and unhealthy diet characterized by high intake of sugar and fats, low consumption of fruits and vegetables are the major causes of non-communicable diseases (NCDs) [8], and strongly linked with early mortality [9,10]. Usually, these risk behaviours exist simultaneously or cluster within individuals [11]. It is argued that lifestyle risk factors within individuals are not random, but more likely to cluster with other unhealthy behaviours [12,13]. Further, when two risk behaviours cluster together with each other more than the other factors, it may suggests that they could be influenced by a common source [14]. Moreover, modifiable risk behaviours for chronic diseases such as excessive use of alcohol, cigarette smoking, obesity and unhealthy diets are unlikely to occur in an entirely uniform manner in a population. That is, it is uncertain whether people can be accurately classify into two groups, as those adapting to a healthy versus those unhealthy lifestyle. For example, certain individuals who engage in more vigorous physical activities tend to consume alcohol more frequently than their inactive counterparts [15]. Also, cigarette smoking is associated with lower rate of obesity among certain individuals [16]. In a study among the US adults, Leventhal et al. (2014) used modifiable risk factors like usage of alcohol, drug, nicotine, current obesity status, and weekly physical activity and found that the adult population clusters into five sub-groups based on the pattern of these modifiable risk factors [14]. Another study in India by Shaikh and Khan (2021),

found that hypertension is more likely to cluster with other modifiable risk behaviours such as smoking, alcohol, chewing tobacco, obesity, and unhealthy diets in both men and women [17]. Atorkey and Owiredua (2021), in their study that identified the clustering of five multiple health risk behaviours, also found that low vegetable and fruit intake, and low physical activity cluster together within an individual, whereas smoking tobacco and alcohol consumption co-occur together forming another cluster [18]. The pattern of clustering of modifiable risk behaviours could also differ by region and community level, as evident from previous studies [17,19]. The clustering of two or more modifiable risk behaviours is of great concern because it can intensify the risk of developing chronic diseases and cardiovascular mortality [20,21], and most intervention measures are specific to a single risk factors. For example, in Asia 43.5 percent of Chinese adults and 37 percent of Korean adults had at least two cardiovascular risk factors [11,22]. Moreover, in India, 35.6 percent of adult men and 10 percent adult women have at least three lifestyle risk factors [17]. It is also found that a combination of smoking and heavy drinking emerged as the riskiest behaviour for all causes of death [23].

The majority of studies reported a higher prevalence of smoking, excess alcohol consumption, physical inactivity, and poor diet among people with diabetes or hypertension than those without diabetes or hypertension [24,25]. Notably, previous studies have examined diabetic or hypertensive patients as a single homogeneous group without considering the possible heterogeneity existing within the population [26]. Most of the existing studies on health risk behaviours have emphasized only changing a single unhealthy behaviour [25,27]. However, interventions that simultaneously target these unhealthy behaviours are necessary from the policy perspective [11].

Existing studies in India on clustering of NCDs risk factors have used intraclass correlation and scoring methods [17,19,28]. However, studies have suggested that LCA is the most appropriate method for explaining the clustering of health risk behaviours [29,30]. LCA is a probabilistic model approach designed for identifying clusters based on dichotomous variables. This study is also an attempt to explore the clustering of NCD risk factors using the LCA approach in Northeastern India. The aims is to identify the latent classes of modifiable risk factors among diabetic and hypertensive patients based on the observed indicator variables such as smoking, alcohol, aerated drinks, overweight or obesity, diabetes, and hypertension. We applied LCA, also to investigate heterogeneity in the population of an individual with diabetes and hypertension based on the responses of observed risk factors. More specifically, the objective is to describe how individuals in Northeast India diagnosed with diabetes or

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hypertension are clustered according to the pattern of observed risk factors and identify the difference between these groups based on socio-demographic characteristics. Information on clustering of health risk behaviours become vital as it guides in designing the disease control programs. Intervention approach that aimed at targeting multiple modifiable risk behaviours in a single program are gaining importance because they are potentially most cost-effective, efficient and may have a great public health impact than the single modifiable risk approaches. Therefore, we hypothesize that the study population diagnosed with diabetes or hypertension is homogeneous with respect to the modifiable risk factors.

Methods

Study location

The study focuses on the Northeastern region (NER) of India comprising eight states, namely Assam, Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, and Tripura (Figure 1). Most parts of the region has a hilly terrain and inhabited mainly by myriad tribes belonging to different cultures and ethnic communities [31]. The region has over 45 million population, which is 3.8 percent of India's population, with a density of 159 persons per km² [32].

Design and Setting

The NFHS-4 (2015-16), a nationally representative large-scale survey, is a cross-sectional study that adopted a stratified two-stage random sampling design for both urban and rural areas, including a systematic mapping and listing of households in the selected primary sampling units (PSUs). The analysis is based on the publicly available data, in which the identity of selected respondents, households, and geocodes of PSUs are concealed [33]. In the first stage, the PSUs were selected based on probability proportional to population size (PPS). Rural PSUs are the villages, while census enumeration blocks (CEBs) formed the PSUs in urban areas. In the second stage, systematic random sampling was done in each PSUs to select households for the sample. At the household level, information were sought from the heads, eligible women age 15 - 49 years, and men age 15 - 54 years, along with their biomarkers and blood samples on a specially designed Dried Blood Spots (DBS). A detailed description of the survey design can be found elsewhere [33].

The data used in this study is the fourth round of the Indian National Family Health Survey (NFHS-4) conducted during 2015-16. The data was downloaded from the DHS website [34].

The NFHS series of surveys has been initiated by the Ministry of Health and Family Welfare, Government of India, and coordinated by the International Institute for Population Sciences, Mumbai.

Sample

The study includes only individuals age 15-49 years who were diagnosed with either diabetes or hypertension, or both. The total sample size is 22,249, of which 3,284 were males, and 18,965 were females for the Northeastern region of India.

Patient and Public Involvement

No patient involved

Measures

Diabetes: Fingerstick blood is collected, and blood glucose level is determined using the FreeStyle Optium H Glucometer. A respondent is considered diagnosed with diabetes if the random blood sugar level is >140mg/dl [33].

Hypertension: Blood pressure (BP) level was measured using an OMRON Blood Pressure measuring device. Three separate blood pressure readings were taken with an interval of 5 minutes between readings. A respondent is considered hypertensive if the systolic blood pressure is \geq 140 mmHg, or diastolic blood pressure \geq 90 mmHg, or if the respondent was taking antihypertensive medication to lower blood pressure at the time of the survey [33].

Overweight or obesity: In this study, we categorized continuous body mass index (BMI) according to the WHO guidelines for the Asian population. A respondent is classified as overweight or obese if BMI is $\geq 23 \text{ kg/m}^2$ [35].

Outcome Variables of Interest

Observed Indicator variables: The observed variables used as latent indicators are cigarette smoking (No=1, Yes=2), Alcohol consumption (No=1, Yes=2), Takes aerated drink (No=1, Yes=2), Overweight or obesity (No=1, Yes=2), Diabetes (No=1, Yes=2), and Hypertension (No=1, Yes=2).

Predictors or Concomitant variables

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Concomitant variables for class determination: The concomitant variables include age, gender, education, marital status, and household wealth index. Figure 2 illustrates the conceptual framework of the study.

Statistical Analysis

Latent Class Analysis (LCA), based on structural equation modelling, is a personcentred analytical approach that allows the identification of homogeneous sub-groups in a heterogeneous population. LCA is similar to cluster analysis because individuals are classifying into homogenous unobserved (latent) groups based on the response pattern to a set of observed variables. However, in cluster analysis, objects are classified based on distance measures, whereas in LCA classification are based on probabilistic and finite mixture modelling approach [36,37]. A latent class model splits the population into mutually exclusive and exhaustive groups that are homogeneous within the groups but differ among them. Several studies have adopted the LCA approach to identify risk factors clustering within the heterogeneous population. In a study by Dey et al (2016), based on seven observed risk factors, LCA was used to classify individuals into two latent class "susceptible to adverse health outcomes groups" and "not susceptible to adverse health outcomes groups" [38]. Another study in China applied LCA to ten observed complications and comorbidities of T2 diabetic patients and categorized the individuals into four latent classes, namely "complications and comorbidity groups", "high risk of complications group", "high risk of comorbidities and Cardio Vascular Disease groups", and "diabetes without complications and comorbidities group" [39]. A study in West Azerbaijan province among the hypertensive patients aged 50 years and above used four indicators such as dietary patterns, physical activity, tobacco use, and high blood pressure control to categorized the hypertensive patients into three latent classes [40].

Latent Class Analysis is an innovative statistical method used to identify the latent classes of homogeneous individuals in a heterogeneous population [39]. The latent class was performed using the six indicators variables mentioned above. LCA uses observed dichotomous indicators to identify the unobserved latent class in a heterogeneous population. To determine the optimal number of latent classes, we examined one to four models. The optimal number of latent classes was chosen based on the model having the smallest Akaike Information Criterion (AIC), Consistent Akaike Information Criterion (cAIC), Bayesian-Schwarz Information Criterion (BIC), adjusted Bayesian-Schwarz Information Criterion (aBIC), and Entropy [41,42]. A combination of parsimony and interpretability model selection

criteria was used to carefully select the number of latent classes so that individuals are allocated to their most likely class. The outputs of the latent class analysis includes the number of latent classes, the latent class probability (i.e., the probability that an individual selected at random belonged to each latent class), and the conditional probability (i.e., the probability that an individual would give a particular response to a specific item of an observed indicator variable given that an individual belongs to a specific latent class).

To determine the association between the concomitant variables (i.e., age, gender, education, marital status, and household wealth index) and the latent class, we apply the onestep technique approach. In this approach, the concomitant variables are included in the latent class regression model, and their coefficient is estimated simultaneously as part of the latent class model [43]. This approach has been demonstrated to provide the best and unbiased coefficient estimates of the concomitant variables as compared to other methods [44]. Statistical analysis was conducted in R statistical software, and LCA was analyze using the poLCA package (Polytomous Variable Latent Class Analysis) [43].

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Results

Descriptive statistics

A total of 22,249 individuals with chronic diseases, i.e., diagnosed with diabetes or hypertension, were included in the analysis (Table 1). Individuals in the age group 45-49 and 15-19 constitute the largest (21.3%) and the lowest (5.0%) respectively in the total sample. Over half (51.2%) of the sample have completed secondary education, 24.6 percent were illiterate, and 79.6 percent were currently married. Further, among the chronic disease patients, the prevalence of smoking, consumption of alcohol, and aerated drinks were 4.2, 14.8, and 68.6 percent respectively. Also, 81.1 percent of the participants reported suffering from hypertension, and 27.7 percent from diabetes. The sample distribution also indicates that chronic condition is much higher among females (86.1%) than males (13.9%), among older ages (age 35+), and among poorer households.

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Background Characteristics	% (n=22,249)
Age	
5-19	5.0
20-24	8.4
25-29	12.2
30-34	15.0
35-39	19.2
40-44	19.0
45-49	21.3
Sex	
Male	13.9
Female	86.1
Education	
Illiterate	24.6
Primary	16.3
Secondary	51.2
Higher Secondary	8.0
Marital Status	
Never married	13.6
Married	79.6
Widowed/Divorced/Separated	6.87
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16.7

34.6 22.4

17.5

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4.2

14.8

68.6

43.3 27.7

81.1

Table 1: Percent distribution of adults of age 15-49 years with chronic condition

Model fit and selection of Latent class

Wealth Index Poorest

Observed Indicators

Take aerated drinks

Overweight or Obesity

Poorer

Middle

Richer Richest

Smoking Drink alcohol

Diabetes Hypertension

The model fit/selection statistics to derive appropriate models are shown in Table 2. We fit the LCA models with classes ranging from 1 to 4. For each LCA model, the model fit indicators BIC, AIC, cAIC, and Entropy were calculated. According to the model fit indicators, a three-Class model has been selected as the best fit model as it has the lowest BIC and cAIC values. Smaller values on each indicator suggest a better model, or a model with few explanatory variables or parameters, and inform the decision of the best model to be retained [45]. Another diagnostic indicator is entropy [46], which indicates how accurately the model defines the classes. In general, an entropy value close to 1.0 is considered as ideal [47], and above 0.8 is also acceptable. An entropy value of 1.0 would indicate that every individual has been perfectly classified within the classes based on the responses of the observed indicators. The three latent classes were labelled as "Diabetic with low-risk lifestyle", "High-risk lifestyle", and "Hypertensive with low-risk lifestyle". Figure 3 portrays the graphical representation of item response probability for the indicator's variables across the latent classes.

No of classes	log-likelihood	Residual df	BIC	aBIC	cAIC	likelihood-ratio	Entropy
1	-69173.1	57	138406.3	138387.2	138412.3	17350.8	-
2	-61315.4	34	122921.0	122828.9	122950.0	1859.2	1.0
3	-58920.2	11	118361.0	118195.7	118413.0	1168.6	0.9
4	-59970.1	-12	120691.0	120452.6	120766.0	2396.1	0.9

 Table 2: Model fit statistics for the latent class models (n=22,249)

Latent class probability and the conditional probability of a "Yes" response for each indicator variables were summarized in Table 3. The last row in Table 3 indicates the probability of class membership in each latent class. About 21 percent of the participants were expected to belong to the Class 1 "diabetic with low-risk lifestyle", 8 percent to Class 2 "high-risk lifestyle", and 71 percent to Class 3 "hypertensive with low-risk lifestyle". Members in Class 1 were likely to report having high blood sugar level (diabetic) and unlikely to smoke cigarette and drink alcohol, and members in Class 3 are likely to report having high blood pressure and unlikely to smoke cigarette or drink alcohol.

Indicator Variables	Diabetic with low- risk lifestyle (Class 1)	High-risk lifestyle (Class 2)	Hypertensive with low- risk lifestyle (Class 3)
Smoking	0.04	0.55	0.02
Drink alcohol	0.12	0.81	0.14
Take aerated drinks	0.76	0.78	0.77
Overweight or Obesity	0.44	0.52	0.51
Diabetic	1.00	0.25	0.11
Hypertensive	0.00	0.88	1.00
Latent class probability	0.21	0.08	0.71

 Table 3: The conditional probability of the response items and the latent class probability for study sample in Northeastern India, NFHS-4, 2015-16

Table 4 presents the distribution of socio-economic and demographic characteristics of the individuals by the three latent classes. Age, gender, education, marital status, and household

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wealth index were statistically found significantly associated with the three latent classes at 1 percent level of significant. The hypertensive with low-risk lifestyle class has the highest proportion of respondents aged 45-49 years, whereas both diabetic with low-risk lifestyle class and high-risk lifestyle class has the highest proportion of respondents aged 35-39 years (19.4%) and 19.5% respectively). Both the diabetic with low-risk lifestyle class (10.6% males vs. 89.4% females) and the hypertensive with low-risk lifestyle class (6.2% males vs. 93.8% females) has the highest proportion of females; males constituted almost 100 percent of the high-risk lifestyle class (99.2% males vs. 0.8% females). Lower proportion of the respondents have completed higher secondary education in case of both diabetic with low-risk lifestyle class (10.5%) and hypertensive with low-risk lifestyle class (8.5%). Marital status shows a similar pattern in all the three classes; higher proportion of married respondents and lower proportion of widowed/divorced/separated respondents (<10%). The Wealth index shows that respondents belonging to the middle quintile constituted the largest proportion in the diabetic with low-risk lifestyle class (27.2%), and high-risk lifestyle class (26.6%). However, respondents belonging to the poorer wealth quintile have the highest proportion of hypertensive with low-risk lifestyle class (29.4%).

Table 4: Percent distribution of diabetic and hypertensive patients age 15-49 years
according to three latent classes by background characteristics, Northeastern India,
NFHS-4, 2015-16

Background Characteristics	"Diabetic with low- risk lifestyle" class (n=4727, 21%)	"High-risk lifestyle" class (n=1828, 8%)	"Hypertensive with low-risk lifestyle" class (n=15,694, 71%)	P-value ^a
Age				< 0.01
15-19	8.08	3.06	4.96	
20-24	8.99	8.37	7.6	
25-29	12.88	13.51	11.93	
30-34	15.30	18.00	15.29	
35-39	19.40	19.53	19.46	
40-44	17.73	19.09	19.04	
45-49	17.62	18.44	21.72	
Gender				< 0.01
Male	10.62	99.18	6.17	
Female	89.38	0.82	93.83	
Education				< 0.01
Illiterate	17.96	11.65	25.17	
Primary	16.50	15.10	15.85	
Secondary	55.05	58.70	50.50	
Higher Secondary	10.49	14.55	8.47	
Marital Status				< 0.01
Never married	19.93	21.55	14.30	
Married	72.75	75.22	78.41	
Widowed/Divorced/Se parated	7.32	3.23	7.30	

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Wealth Index				< 0.01
Poorest	10.94	12.14	12.94	
Poorer	26.06	24.84	29.43	
Middle	27.23	26.64	26.30	
Richer	22.49	23.34	21.25	
Richest	13.29	12.04	10.07	
Total	100.0	100.0	100.0	

Note: ^aBased on chi-squared tests of association.

Covariates predicting latent class membership

Table 5 summarized the odds ratios (OR) results from the latent regression model. Compared with respondents in the 15-19 years age group, those in the 20-29 age group were 4.1 times (OR=4.10; p-<0.01) more likely to belong to class 2 (high-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Similarly, compared with respondents in the 15-19 years age group, those in the 45-49 age group were 1.7 times (OR=1.73; p-<0.01) more likely to belong to class 3 (hypertensive with low-risk lifestyle) than to class 1 (diabetic with low-risk lifestyle). Also, we observed that the odds of being in class 3 increases with the age of the respondents. With respect to males, females were less likely (OR=0.002; p-<0.01) to belong to class 2 but more likely (OR=1.46; p-<0.01) to belong to class 3. Higher odds of being in class 2-3 than to class 1 was observed among the married respondents (OR=1.54). Similarly, widowed/divorced/separated were more likely to be in class 2 (OR=3.35; p-<0.01), but less likely to be in class 3 (OR=0.98; p-<0.01). Moreover, compared to the illiterate respondents, those with higher secondary education were less likely to belong to class 3 than to class 1 (OR=0.69; p-<0.01).

co	ovariates among individuals age 15-49 years, Northeastern India, NFHS-4, 2015-16				
	Background Characteristics	Class 2 vs Class 1		Class 3 vs Class 1	
	Background Characteristics	Odds Ratio	S. E	Odds Ratio	S. E
	A = 2				

Table 5: The odds for various latent classes of lifestyle behaviours and their associated

Dackgi bund Characteristics	Odds Ratio	S. E	Odds Ratio	S. E
Age				
15-19	Ref		Ref	
20-24	4.10 ***	0.25	1.27 **	0.09
25-29	5.10 ***	0.25	1.34 ***	0.09
30-34	5.70 ***	0.26	1.42 ***	0.09
35-39	3.53 ***	0.26	1.42 ***	0.09
40-44	3.82 ***	0.27	1.51 ***	0.09
45-49	3.46 ***	0.27	1.73 ***	0.09
Gender				
Male	Ref		Ref	
Female	0.002 ***	0.34	1.46 ***	0.07

Education				
Illiterate	Ref		Ref	
Primary	1.03	0.19	0.73 ***	0.06
Secondary	1.08	0.17	0.79 ***	0.05
Higher Secondary	0.70	0.21	0.79 ***	0.08
Marital Status				
Never married	Ref		Ref	
Married	1.54 **	0.15	1.16 **	0.06
Widowed/Divorced/Separated	3.35 ***	0.35	0.98	0.08
Wealth Index				
Poorest	Ref		Ref	
Poorer	0.90	0.18	1.00	0.06
Middle	1.02	0.18	0.87 **	0.07
Richer	1.14	0.19	0.86 *	0.07
Richest	1.13	0.22	0.69 ***	0.08

Ref: Reference group; ***p-value<0.01; **p-value<0.05; *p-value<0.1; S.E: Standard Error; Reference group: Class 1

Discussion

This study is the first attempt in Northeastern India, a region characterized by a seemingly homogenous racial group but inhabited by ethno-lingually diverse sub-populations, that applied latent class analysis to provide evidence about the pattern of modifiable risk factors among people suffering from diabetes or hypertension. Based on the observed modifiable health risk behaviours, the LCA suggests presence of three classes of respondents with diabetes or hypertension: "diabetic with low-risk lifestyle", "high-risk lifestyle", and "hypertensive with low-risk lifestyle". The findings portray that the 22,249 odd diabetic or hypertensive persons in the region can be categorized into three groups or classes, with homogeneity in their characteristics within the group but heterogeneous between the groups. One of the three latent classes has a 100 percent likelihood of having one of the risk factors combined with a low and moderate probability of having the other five risk factors. Each of the classes exhibit a unique risk factor configuration, and socio-economic and demographic profiles from one another. Thus, chronic diseases prevention programmes that specially target and reach out to the at-risk sub-populations will be beneficial and effective, as illustrated in this analysis (Table 3 and 5).

More than 70 percent of the respondents belong to the class "hypertensive with lowrisk lifestyle" have their blood pressure level higher than normal and less likely to smoke and use alcohol. Evidence from a large body of existing literature supports that cigarette smoking leads to an immediate increase in blood pressure level and heart rate [48]. The effect of cigarette smoking on blood pressure and heart rate is largely due to the nicotine content in the cigarettes [48]. However, studies also found a significant elevation in blood pressure and an increase in the prevalence of hypertension following smoking cessation [49,50], which could possibly be due to post-cessation weight gain [48,49]. Green et al. (1986) had concluded that smoking cessation in itself is not likely to result in a lowering blood pressure but on the contrary it may result even in higher blood pressure [51]. Moreover, about 8 percent of the respondents belonging to the "high-risk lifestyle" class mostly drink alcohol and smoke cigarettes. This cooccurrence of alcohol use and cigarette smoking have been well documented in the existing studies [52,53], and evidence suggest that a common genetic trait play a role in the cooccurrence of smoking and alcohol use [54,55]. Epidemiological studies have also shown that individuals who are dependent on nicotine are more than four time more likely to be dependent on alcohol. Similarly, individuals who are dependent on alcohol are also more than three times more likely to be dependent on nicotine with reference to the general population [56]. Stress is another factor that influences use of tobacco and alcohol. For example, people who drink alcohol are most likely to smoke in an attempt to overcome stress [57]. Literature also suggest cross tolerance effect between alcohol and tobacco. It is found that the stimulating effect of nicotine in tobacco is restrained by the sedating effect of alcohol, which entices smokers to drink more alcohol [58]. Alcohol's sedating effect reduces the physiological effect of nicotine, thus increasing the consumption of tobacco.

In all the three identified classes, a vast majority of diabetic or hypertensive persons appear to have a habit of consuming aerated drinks and an uncontrolled body weight. Studies suggest that sugar-sweetened beverages intake is the major contributor to weight gain and can increase the risk of T2 diabetes and hypertension [59,60]. Cross-sectional studies acknowledge the positive association between overweight and obesity with the consumption of aerated drinks or sugar-sweetened beverages. For example, studies infer that women who consumed sweetened beverages more than once a week were more likely to be overweight than those who consumed sweetened beverages less than once a week [61]. Other studies found that women who consumed sugar-sweetened beverages regularly were heavier by 0.2 kg than the nonconsumers [62]. The intake of sodas sweetened with high-fructose corn syrup is associated with hypertension among adolescents population [63]. Also, a spurt in the prevalence of hypertension have been observed among individuals who consumed more than average amount of fructose [64]. Evidence from a cross-sectional study in Northeast India supports the positive correlation between overweight or obesity with diabetes and hypertension [26]. The plausible explanation is that both sugar sweetened beverages and artificial sweetened beverages are associated with the development of metabolic derangements that in turn might lead to elevated

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blood pressure [65]. High intake of sugar-sweetened beverages contributes to a higher total energy consumption, which increases energy intake without an increase in energy expenditure certainly results in weight gain. There is no dearth of scientific evidence which support the notion that decreasing aerated drinks consumption reduces the prevalence of overweight and obesity.

As observed in a previous study [66], this study also found that those aged 20 years and above are more likely to be in the 'high-risk cluster' than those below 20 years. Studies have elucidated that the adolescence or teenage stage is just the initial stage when an individual starts using or exposed to alcohol or tobacco (smoking) products. However, as this behaviour becomes a habit later on, it subsequently accentuates the intensity of substance (ab)use among older adults [67,68]. Also, it is well documented that initiation of smoking and drinking alcohol at an early age is associated with the number of cigarettes smoked and the quantity of alcohol consumed per day in adult age. According to Investigator (1991) and Dawson et al. (2008), individuals who began to smoke or drink before the age of 20 years were most likely to consumed a large volume of alcohol and smoked more cigarettes per day as compared to those who started after the age of 20 or above [69,70]. Further, compared to young adults, older adults were more likely to report high blood pressure and less likely to smoke or drink alcohol. One reason could be the existing condition of high blood pressure; an older adult was most likely to have taken a precaution by lowering or quitting smoking and alcohol consumption to prevent further deterioration of health. Evidence from a recent study among older adults demonstrated that the main reason for smoking cessation attempt was the motivation towards better health [71]. Hypertensive smokers were encouraged to quit smoking because of the risk of developing a severe form of hypertension such as malignant and renovascular hypertension [72]. Gender factors are also found to be significantly associated with class 2 "high-risk lifestyle" and 3 "hypertensive with low-risk lifestyle". Consistent with the previous studies, in this study also, female respondents were less likely to be in the high-risk cluster than males [73]. One primary reason stated is that smoking and drinking alcohol by women is not socially and culturally accepted by many [74], and women are more concerned about their health and tend to avoid unhealthy lifestyle behaviours [75]. In our study, individuals from a wealthier household with higher education were less likely to belong to a cluster of hypertensive with low substance use. An individual with higher education and better income can afford to pay for a healthier lifestyle, including regular physical exercise, accessibility to advanced and quality healthcare services, as such efforts may reduce the risk of hypertension [76,77]. Being

widowed/divorced/separated tend to increase the likelihood of falling into the high-risk cluster. Substance use by marital status indicated that widowed or divorced individuals are most likely to consumed alcohol, cigarette, and marijuana as compared to singles [78,79].

A search of similar studies indicates that no study in India or Northeast India has examined the clustering of health risk factors using the latent class approach. However, our study has some limitations. Firstly, the cross-sectional design of the study restricts us to measure the causal effect. Second, due to the dichotomous response on alcohol consumption, we cannot measure the quantity of alcohol an individual consumed. Lastly, information on social groups and occupations could not be included in the analysis because of the large number of missing cases in these variables.

Conclusion

In Northeastern India, as this study illustrates, there are three classes of modifiable risk factors closely related to the risk of chronic diseases (diabetes and hypertension). In addition, the study also identified factors that uniquely distinguished the identified classes. The intake of aerated drinks and obesity are the common modifiable risk factors in all three classes. As an initiative to healthy lifestyle behaviours, the findings suggest that males should control smoking and alcohol consumption, while females should control body weight and blood pressure. Further, we found that marital status and gender could be the catalyst to prevent high-risk smoking and alcohol drinking in Northeastern India. Also, the study observes smoking and alcohol use are the two modifiable risk behaviours, which tends to co-occur within an individual. Therefore, it is recommended that policy and intervention programmes in Norteastern India that promote healthy lifestyles should focus on targeting multiple modifiable risk behaviours that are most likely to co-occur within an individual. On the other hand, awareness about adapting to healthy diets and weight control along with physical exercises should be promoted with rigour in the region.

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Patient consent for publication: Not applicable

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Data availability statement: Data stored and maintained by the Demographic Health Survey office, and available to public at <u>https://dhsprogram.com/data/dataset/India_Standard-DHS_2015.cfm?flag=1</u> upon request.

Word count: 4464

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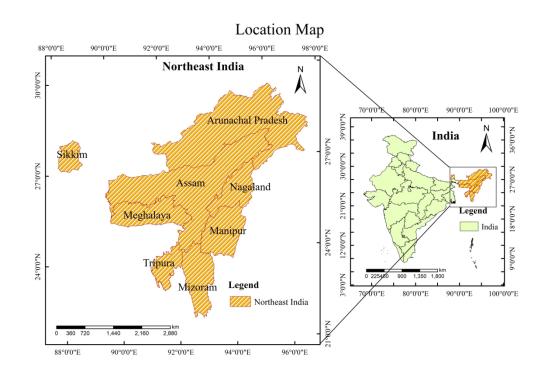
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Figure 1: *Map showing the location of the Study area. Source: Authors* Figure 2: *Conceptual framework of the study. Source: Authors*

Figure 3: Item response conditional probability across the latent classes. Source: Authors

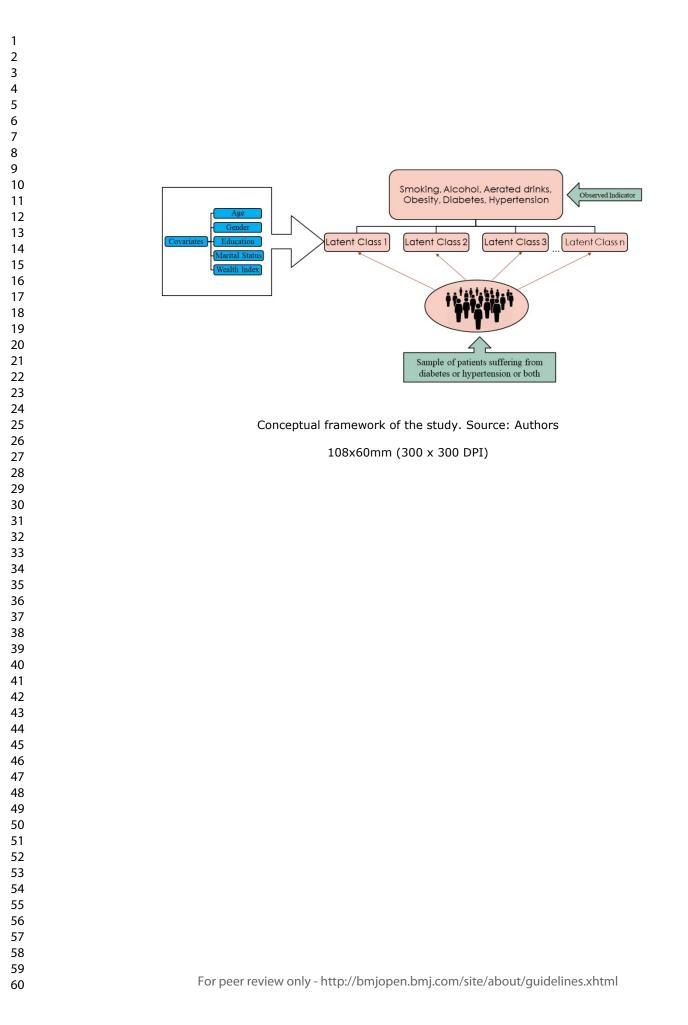
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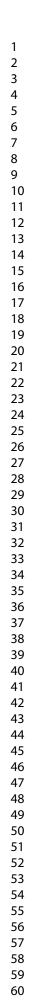


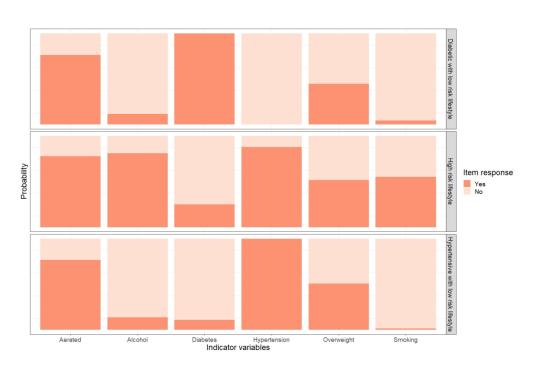
Map showing the location of the Study area. Source: Authors

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Item response conditional probability across the latent classes. Source: Authors

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Section/Topic	ltem #	Recommendation	Reported on page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods		5	
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Not applicable
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	9
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Not applicable
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	Not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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