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ORIGINAL RESEARCH

# Trajectories of Treatment Burden Among Primary Care Patients with Long-Term Conditions in Southern China: A Latent Class Growth Analysis

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**Background:** Treatment burden is a patient-centred, dynamic concept. However, longitudinal data on the changing pattern of treatment burden among patients with one or more long-term conditions (LTCs) are relatively scanty. We aimed to explore the longitudinal trajectories of treatment burden and associated risk factors in a large, patient population in primary care settings.

**Methods:** We analysed data from 5573 primary care patients with long-term conditions (LTCs) recruited using a multistage sampling method in Shenzhen, southern China. The treatment burden was assessed by the Mandarin Chinese version of the Treatment Burden Questionnaire (TBQ). We used latent class growth mixture modelling (LCGMM) to determine trajectories of treatment burden across four time points, ie, at baseline, and at 6, 12, and 18 months. Predictors of trajectory classes were explored using multivariable logistic regression analysis.

**Results:** The mean TBQ scores of patients with a single LTC (n = 2756), 2 LTCs (n = 1871), 3 LTCs (n = 699), and ≥4 LTCs (n = 247) were 18.17, 20.28, 21.32, and 26.10, respectively, at baseline. LCGMM identified three discrete classes of treatment burden trajectories over time, ie, a high-increasing class, a low-stable class, and a high-decreasing class. When controlling for individual-level factors including age, education, monthly household income per head, smoking, alcohol consumption, and attendance in health education, patients who had a clinical diagnosis of 3 LTCs (adjusted odds ratio [aOR] = 1.49, 95% CI = 1.21–1.86, $P < 0.001$) or ≥4 LTCs (aOR = 1.97, 95% CI = 1.44–2.72, $P < 0.001$) were more likely to belong to the high-increasing class. Sensitivity analysis using propensity score methods obtained similar results.

**Conclusion:** Our study revealed the presence of discrete patterns of treatment burden over time in Chinese primary care patients with LTCs, providing directions for tailored interventions to optimise disease management. Patients with 3 or more LTCs should receive close attention in healthcare delivery as they tend to experience a greater treatment burden.

**Keywords:** longitudinal trajectories, treatment burden, long-term conditions, multimorbidity, risk factors

## Introduction

Treatment burden has been defined as the 'work' (eg, attending appointments, undergoing medical tests, taking and managing medications, self-monitoring, and changing lifestyles) of being a patient and its impact on their daily functioning and well-being.[1–4] The burden of treatment is often associated with adherence to therapeutic care, particularly in patients with long-term conditions (LTCs) that require continuous and lifelong treatment.[4–7] From a multimorbidity perspective, disease-centred clinical practice guidelines and quality metrics often fail to take into



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account the circumstances of patients with two or more LTCs,[8] who are likely to suffer from overwhelming treatment burden.[9] It has been shown that an additive, uncoordinated, and often contradictory treatment task could serve as a trigger for the increased burden placed on patients.[6,7]

In routine practice, some patients may persevere with their healthcare regime despite tremendous workload, while others may falter even when relatively unencumbered.[10] The differences in the way patients manage their health could result in significant disparities in the utilisation of care, health and functional status, and quality of life.[11] A practical model of patient complexity has been proposed, positing that personal, social, and clinical aspects of patients' experiences may serve to complicate factors that appear and accumulate over time.[12] It highlights a need for understanding the mechanism driving the complexity of treatment burden in the delivery of patient-centred care.[13] For example, a prospective survey study explored longitudinal patterns of treatment burden in patients with multimorbidity in a Western population.[14] However, such data are relatively scanty in upper-middle-income countries in the East such as China. Furthermore, changes in the estimates of treatment burden between patients with a single LTC and those with two or more LTCs may differ over time.[7,14]

In the global context of primary care transformation,[15] studies to assess patients' experiences with treatment and factors associated with treatment burden in the delivery of care have become an emerging area of research interest.[16] Some studies have shown that treatment burden is more pronounced in patients with more LTCs,[7,17,18] whereas others have reported non-significant differences in burden trajectory classification by the number of diagnosed chronic conditions.[14,19] The inconsistency of the findings may be explained by methodological heterogeneity in dealing with potential confounders.[20] Propensity scoring matching (PSM) has been used with increasing frequency to reduce bias by mimicking the effect of randomisation with observational data.[21] This would allow for comparing treatment burden among patients with different numbers of LTCs who have approximately similar distributions of baseline covariates within the same stratum.[22] Furthermore, existing efforts tend to focus on reducing treatment burden through the modification of workload-related factors, eg, such as minimising the total travel time and/or providing social support for self-management.[7,14] Such an approach is often accompanied by concurrent lifestyle management and health education,[5,23–26] yet short-term beneficial effects in reducing treatment burden remain to be closely monitored in the long term. The present study therefore sought to identify the latent trajectory classes of treatment burden and its relation to the number of LTCs and other factors in a longitudinal sample of Chinese patients in primary care.

# Methods

## Study Design and Sample

We conducted a prospective, observational study among primary care patients in government-owned and hospital-managed community health centres (CHCs) in Shenzhen, southern China. These CHCs are primary care facilities that function as outreach clinic outside of the hospital setting, providing both Western and traditional Chinese medicine services.[27,28] Patients who had enrolment registration with the CHCs were recruited from a total of 33 CHCs managed by a tertiary-level hospital, following a multistage sampling design. We aimed to invite approximately 15% of adult patients who had at least one LTC to participate in our survey on the day of their primary care visits, with a modified systematic random sampling that was used in previous studies.[28–30] All primary care service users, except those who were passers-by or who were unable to communicate due to serious mental disorders, were eligible for participation to maximise the diversity of the selected sample of study patients. Face-to-face surveys were conducted at baseline, and at 6, 12, and 18 months.

## Study Variables and Measurements

We used a self-designed questionnaire, including items derived from our previous research,[28–30] to collect patient-level information on sociodemographic characteristics, lifestyle behaviours, service utilisation and attendance in health education, use of medications, and the number of physician-diagnosed LTCs. Information on the disease condition was captured from medical records and was coded following the International Classification of Diseases (ICD-10). Given the absence of consensus methods to define multimorbidity,[31] we used a simple unweighted enumeration of the number

of LTCs, following a UK definition and our previous study.[30,32] A panel consisting of two general practice (GP) physicians, two public health professionals, and an epidemiologist rated the relevancy and clarity of each questionnaire item. The content validity index was calculated using a four-point Likert-type scale. All items were rated as quite (three-point) or highly (four-point) relevant and clear in the panel review.

The primary outcome of the study was treatment burden, measured by the 15-item Treatment Burden Questionnaire (TBQ), which was originally developed in French patients with multiple chronic conditions in hospitals and GP clinics.[33] The questionnaire involves a variety of treatment workloads concerning medication management, self-monitoring, laboratory tests, doctor visits, need for organisation, administrative tasks, lifestyle changes and social impact.[33,34] The original questionnaire was translated into English and was validated for patients with one or more chronic conditions.[34] We have been commissioned by the Mapi Research Trust to develop a Mandarin Chinese version of TBQ (version TBQ_AU1.0_cmn-CN_RC) in an earlier study,[30] based on the English version. We adopted a standard forward-and-backward translation methodology and linguistic validation process to improve clinical and cultural relevance. There were no additions or deletions of the original TBQ items in the translation, despite minor adaptations made to ensure the cultural relevance and contextual appropriateness of TBQ in China. Apart from the clinician review, we also assessed psychometric properties of the instrument. Factorial validity of the Chinese version of TBQ, assessed by scree plots, favoured a two-dimensional solution, which explained 71.3% of the total variance. The overall Cronbach's α was 0.884, and the test–retest intraclass correlation coefficients of individual item scores ranged from 0.725 to 0.846.[30] The evaluation suggested good reliability and validity of TBQ for measuring treatment burden in the Chinese patients.

All interviewers attended training sessions held by study investigators at each CHC before the commencement of data collection. A pilot study was conducted to ensure that all questionnaire items could be answered without any ambiguity. Double entry verification was independently performed using EpiData 3.1 to improve data accuracy. In this observational study, data were collected on-site at CHCs during patients' clinical visits. Participation in the survey was on a voluntary basis, without financial incentives. Mean imputation was applied to missing data of TBQ by taking the mean of all available scores when less than 50% of items had missing values. The average of all TBQ item scores, after imputation if needed, was converted into a global scale that ranged between 0 and 100,[14] with higher global scores indicating greater treatment burden.

## Statistical Analysis

Trajectories of treatment burden were assessed using the latent class growth mixture modelling (LCGMM). It is a semi-parametric technique that permits the identification of distinct clusters of individuals with similar patterns of change in TBQ over time.[35] The population heterogeneity of individual differences in change within the data is summarised by a finite set of polynomial functions, each corresponding to a discrete trajectory.[36] In contrast to the classical mixed effect regression models in which potential within-group trajectory variations are absorbed by the model's random effects, the LCGMM assumes that distinct subpopulations in the study sample have different development trajectories.[37] Based on existing literature,[11,12,14] we assumed a linear pattern of change in TBQ, which may either increase or decrease at varying magnitudes or remain stable over time.[35]

Patients who had treatment burden assessed at baseline, and at least two follow-up assessments of treatment burden, were included in the analysis. A maximum likelihood method with a general quasi-Newton algorithm was applied for estimating model parameters.[38] We hypothesised that there were at least two discrete classes of TBQ trajectories at follow-up. We first determined a one-class model, thus assuming one underlying population. An additional class was added one at a time subsequently, with model fit indices tested at each step.[39] We considered multiple fit statistics, ie, Bayesian Information Criterion (BIC), entropy values, and the Vuong-Lo-Mendell-Rubin (VLMR) likelihood ratio test.[40–42] The BIC penalises −2 log likelihood by adding the number of estimated parameters multiplied by the log of the sample size, which tends to favour more parsimonious models, with lower BIC values indicating better model fit.[43] The entropy statistic indicates the accuracy of classification into latent classes, with higher values indicating better classification.[39] A significant *P* value on the VLMR test indicates that the model with *k*-1 fewer classes should be rejected in favour of the model with at least *k* classes (where *k* is the current number of classes).[44] We also took into account parsimony and interpretability when determining the number of classes. Other considerations included average

posterior probabilities (ie, the probability that an individual is classified into a given class) ≥0.80, and no less than 2% of the total count in a class.[41] The latent growth curve modelling (LGCM) was used to analyse the patterns of changes in TBQ scores over time in each class after determining the best fitting latent class solution.

Patient characteristics were presented as mean (standard deviation) and number (%) of patients for numeric and categorical variables, respectively. The chi-square test was used for comparisons of patient profiles, in a categorical approach, across different trajectory classes. Variables that were statistically significant in bivariate analyses were entered in multivariable logistic regression models to test for their association with trajectory classes of TBQ. Sensitivity analyses were performed to ensure the robustness of our findings. We calculated the average marginal effects (AMEs), ie, the average difference across patient groups by the number of LTCs in the predicted probability of a given trajectory class of treatment burden with other covariates held constant.[45] The AME coefficients were then converted to percentages to reflect the magnitude of differences across groups by the number of LTCs. We also employed the inverse probability of treatment weighting (IPTW) following the propensity score matching (PSM) to address confounding,[21] thus yielding a weighted sample with balanced covariates to examine directly the association between the number of LTCs and the changes in patients' treatment burden over time.

Statistical significance level was set at $P < 0.05$. LCGMM and LGCM were performed using Mplus 8.3. Inverse probability weighting for multinomial variables was performed with the package "ipw",[46] using R 4.1.2. All other analyses were conducted in Stata 15.1.

## Ethical Considerations

All patients provided written informed consent. Data were anonymised in the dataset to protect patient privacy. Ethics approval was granted by the School of Public Health Biomedical Research Ethics Review Committee at Sun Yat-Sen University in accordance with the Declaration of Helsinki 2013.

# Results

## Study Population

We included a total of 5573 patients who had treatment burden assessed at baseline, and at least two follow-up visits. The mean age of the study participants was 54.43 (standard deviation [SD] 12.12) years, and slightly over half (53.31% [2971/5573]) were male. Most participants were married (95.08%), living with family members or carers (90.65%), and migrants (89.52%). The majority of participants were non-smokers (79.10%) or had no drinking habits (77.95%). More than half (59.66%) of patients travelled less than 15 minutes to the CHC. Slightly over 1 in 10 (12.43%) patients had hospital admission in the past 12 months. Around one-fifth (21.71%) of patients attended health education. The proportions of patients who had been diagnosed with a single LTC, two or more LTCs, 2 LTCs, 3 LTCs, and ≥4 LTCs were 49.45%, 50.55%, 33.57%, 12.54%, and 4.44%, respectively (Table 1).

## Treatment Burden Scores

The mean TBQ scores of patients with 1 LTC (n = 2756), 2 LTCs (n = 1871), 3 LTCs (n = 699), ≥4 LTCs (n = 247) were 18.17, 20.28, 21.32, and 26.10, respectively, at baseline. Overall, scores in all patients increased from baseline to 6 months, remained stable between months 6–12, and then decreased after 12 months (Figure 1A). Among patients with a single LTC, the TBQ scores had a sharp increase from baseline to 6 months, followed by a decreasing trend between months 12–18; while in their counterparts with 2 or more LTCs (ie, multimorbidity), the TBQ scores increased mildly over the first 12 months and then declined, with higher treatment burden than those with the absence of multimorbidity at all time points (Figure 1B; Figure 1C). In patients with 2 LTCs, the TBQ scores increased over the first 6 months but decreased steadily thereafter (Figure 1D). In patients with 3 LTCs, the TBQ scores increased with subtle fluctuations during the follow-up period (Figure 1E). In patients with 4 or more LTCs, we observed a mixed pattern in the change of TBQ scores, reaching a peak at 12 months (Figure 1F).

**Table 1** Characteristics of Study Participants (N = 5573)

| Characteristics | N (%) |
|---|---|
| Age, years, mean (SD) | 54.43 (12.12) |
| Age groups (years) | |
| <30 | 51 (0.92) |
| 30–39 | 531 (9.53) |
| 40–49 | 1522 (27.31) |
| 50–59 | 1533 (27.51) |
| 60–69 | 1301 (23.34) |
| 70–79 | 530 (9.51) |
| ≥80 | 105 (1.88) |
| Sex | |
| Male | 2971 (53.31) |
| Female | 2602 (46.69) |
| Marital status | |
| Single | 121 (2.17) |
| Married | 5299 (95.08) |
| Divorced /Widowed | 153 (2.75) |
| Living situation | |
| Living with family members/carers | 5052 (90.65) |
| Living alone | 521 (9.35) |
| Household registration | |
| With "Hukou" | 584 (10.48) |
| Without "Hukou" | 4989 (89.52) |
| Education level | |
| College and above | 481 (8.63) |
| Senior secondary school | 1219 (21.87) |
| Junior secondary school | 2131 (38.24) |
| Primary school or below | 1742 (31.26) |
| Medical insurance | |
| Insured | 2998 (53.80) |
| Uninsured | 2575 (46.20) |
| Employment status | |
| Employed | 2996 (53.76) |
| Unemployed | 683 (12.26) |
| Retired | 1894 (33.98) |
| Monthly household income per head | |
| Less than CNY3000 | 551 (9.89) |
| CNY3000 and above | 2951 (52.95) |
| Unreported | 2071 (37.16) |
| Occupation | |
| Public service | 458 (8.22) |
| Enterprise employment | 1151 (20.65) |
| Self-employment | 1807 (32.43) |
| Farming | 574 (10.30) |
| Skilled worker | 1583 (28.40) |
| Cigarette smoking | |
| Non-smoker | 4408 (79.10) |
| Smoker | 780 (14.00) |
| Ever-smoker | 385 (6.90) |
| Alcohol consumption | |
| Non/seldom drinker | 4344 (77.95) |
| Regular drinker | 955 (17.14) |
| Ever-drinker | 274 (4.91) |

(*Continued*)

**Table 1** (Continued).

| Characteristics | N (%) |
|---|---|
| Travel time to the nearest CHC, minutes | |
| <15 | 3325 (59.66) |
| 15–30 | 1853 (33.25) |
| >30 | 395 (7.09) |
| Hospitalisation in the past 12 months | |
| Yes | 693 (12.43) |
| No | 4880 (87.57) |
| Attendance in health education | |
| Yes | 1210 (21.71) |
| No | 4363 (78.29) |
| Number of medications used | |
| 0 | 1385 (24.85) |
| 1 | 2349 (42.15) |
| 2 | 1318 (23.65) |
| 3 | 379 (6.80) |
| ≥4 | 142 (2.55) |
| Number of LTCs | |
| 1 | 2756 (49.45) |
| 2 | 1871 (33.57) |
| 3 | 699 (12.54) |
| ≥4 | 247 (4.44) |

**Abbreviations**: CHC, community health centre; LTCs, long-term conditions.

## Longitudinal Trajectories of Treatment Burden

We tested for five classes of TBQ change, and a three-class model was supported by multiple fit statistics while considering all relevant factors. Entropy values ranged between 0.727 and 0.858, and all models met the sample size count criteria. The VLMR test indicated a 2- or 3-class model, while the BIC statistic favoured a 3-class model (Table 2; Figure 2). The high-increasing class (n = 872, 15.65% of total sample) was characterised by a high intercept (mean intercept = 1.129, $P < 0.001$) and a significant positive slope (mean slope = 0.382, $P < 0.001$). The low-stable class (n = 4474, 80.28% of total sample) was characterised by a relatively lower intercept (mean intercept = 0.922, $P < 0.001$) and a mild slope (mean slope = −0.079). The high-decreasing class (n = 227, 4.07% of total sample) was characterised by a significant high intercept (mean intercept = 3.198, $P < 0.001$) and a significant negative slope (mean slope = −0.790, $P < 0.001$).

## Factors Associated with Trajectory Classes of Treatment Burden

Patients' characteristics with respect to education level, monthly household income, smoking and drinking status, attendance in health education, and the number of LTCs differed across the three distinct trajectory classes (Supplementary Table S1). The univariate logistic regression analyses showed that patients who had lower education level, higher household income per head, and more LTCs were more likely to be in the high-increasing (*versus* low-stable) treatment burden class, and that patients who were older, had alcohol consumption history, and did not attend health education were more likely to be in the high-increasing (*versus* high-decreasing) treatment burden class (Supplementary Table S2). The results remained consistent when controlling for individual-level covariates. Compared with patients with a single LTC, those who had 3 LTCs (adjusted odds ratio [aOR] = 1.49, 95% confidence interval [CI]=1.21–1.86, $P < 0.001$; AME = 5.56) or had ≥4 LTCs (aOR = 1.97, 95% CI = 1.44–2.72, $P < 0.001$; AME = 9.79) were more likely to fall within the high-increasing (*versus* low-stable) treatment burden class (Table 3). In the sensitivity analysis, the use of PSM and IPTW for covariate balancing yielded similar results. Compared with patients having a single LTC, those with 3 LTCs (aOR = 1.46, 95% CI = 1.17–1.83; $P < 0.001$) or had ≥4 LTCs (aOR = 1.77, 95% CI = 1.24–2.51, $P < 0.001$) had a higher likelihood of belonging to the high-increasing treatment burden class (Figure 3).

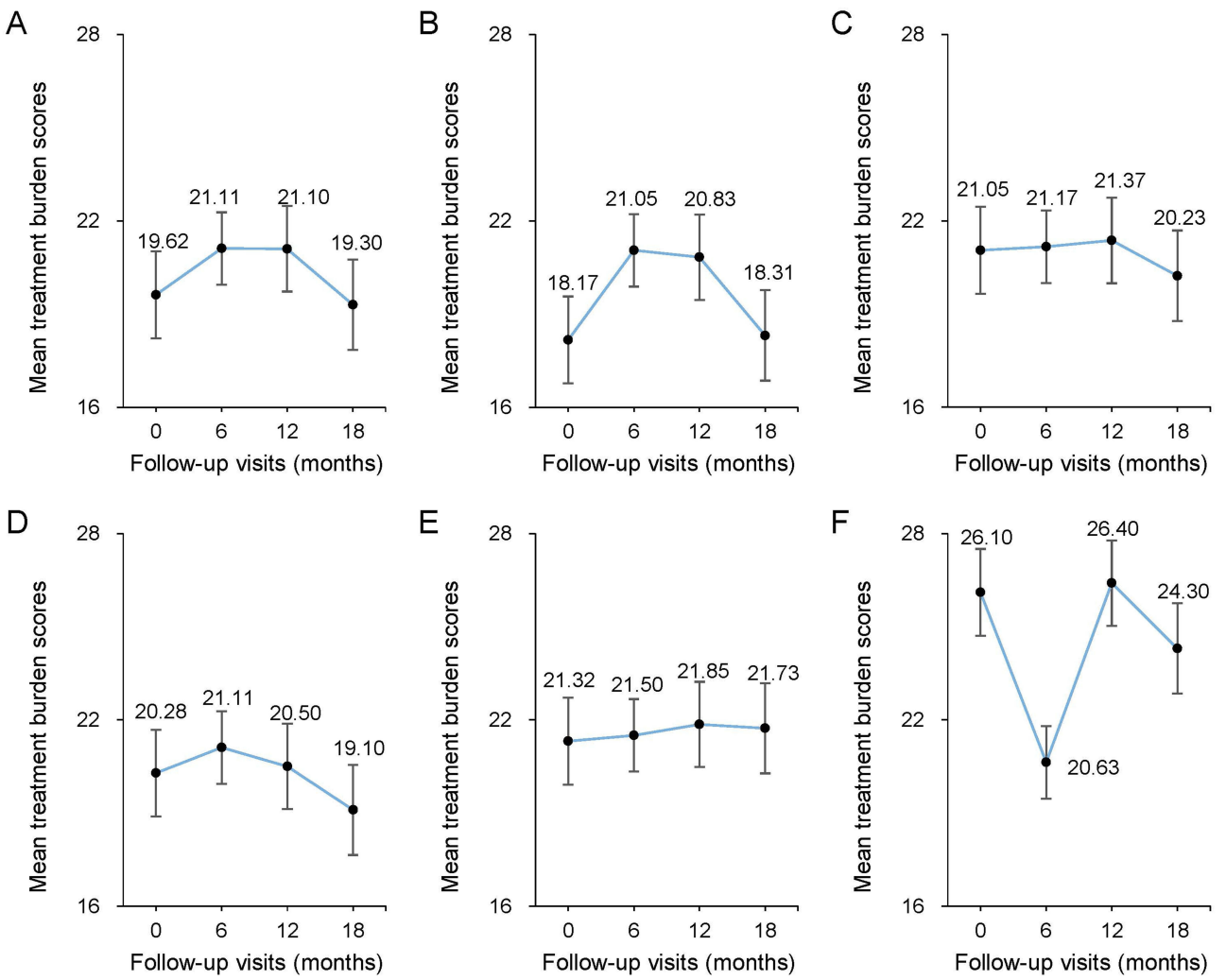


**Figure 1** Mean treatment burden scores by LTCs during follow-up.
**Notes**: (**A**) All patients; (**B**) Patients with a single LTC; (**C**) Patients with two or more LTCs; (**D**) Patients with 2 LTCs; (**E**) Patients with 3 LTCs; (**F**) Patients with ≥4 LTCs. Error bars represent 95% confidence intervals.
**Abbreviation**: LTC, long-term condition.

# Discussion

## Main Findings

The present longitudinal study examined the latent trajectory of treatment burden in a Chinese primary care population, including patients with a single LTC (49.45%), and with multimorbidity (50.55%). The increase in the number of LTCs was accompanied by the rise in treatment burden at follow-up. Three trajectories of treatment burden over time, ie, high-increasing, low-stable, and high-decreasing, were identified via LCGMM. When adjusting for individual-level covariates, patients who had greater numbers of LTCs were prone to experience a high-increasing (versus low-stable) treatment burden. The use of PSM and IPTW for covariate balancing in the sensitivity analysis yielded similar results.

## Relationship with Other Studies

Two recent follow-up studies reported similar patterns of changes in treatment burden over time in adult patients living with multimorbidity, despite the use of different measurement tools for treatment burden. The study in the United Kingdom, using the Multimorbidity Treatment Burden Questionnaire (MTBQ) in 300 patients, reported that participants experienced either an increase or decrease in treatment burden over 2.5 years of follow-up.[7] The other study in the United States, using the Patient Experience with Treatment and Self-management (PETS) measure in nearly 400 patients,

**Table 2** Fit Indices Used for Deriving the Optimum Number of Treatment Burden Trajectories Using LCGMM

| Number of classes | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Model fit | | | | | |
| BIC[a] | 52458.44 | 51110.81 | 50525.97 | 50148.95 | 49785.89 |
| Entropy[b] | – | 0.858 | 0.777 | 0.727 | 0.781 |
| VLMR[c] | – | 0.002 | 0.027 | 0.251 | 0.326 |
| Number of patients in each class (%) | | | | | |
| 1-class | 5573 (100.00) | 463 (8.31) | 872 (15.65) | 842 (15.11) | 1351 (24.24) |
| 2-class | – | 5110 (91.69) | 4474 (80.28) | 3907 (70.10) | 216 (3.88) |
| 3-class | – | – | 227 (4.07) | 633 (11.36) | 3101 (55.64) |
| 4-class | – | – | – | 191 (3.43) | 781 (14.01) |
| 5-class | – | – | – | – | 124 (2.23) |

**Notes**: [a]lower BIC values indicate better fit. [b]Entropy value ranges from 0 to 1. A higher value indicates a more accurate classification into the latent classes. [c]Vuong-Lo-Mendell-Rubin likelihood ratio test. A significant *P* value indicates that the model with *k*-1 fewer classes should be rejected in favour of the model with at least *k* classes.

**Abbreviations**: LCGMM, latent class growth mixture modelling; BIC, Bayesian information criterion; VLMR, Vuong-Lo-Mendell-Rubin.

identified a 2-class model for treatment workload, ie, consistently high and consistently low, and a 3-class model for the impact of treatment on quality of life, ie, consistently high, consistently low, and increasing over time, respectively, at a 2-year follow-up.[14] Compared to previous studies that adopted mailed surveys in multimorbid patients, our study used face-to-face interviews, had a much larger sample size, and included both patients who had a single LTC and their counterparts who had multimorbidity. Our results by using a validated, Chinese version of the TBQ measure were broadly consistent with previous findings. A high-decreasing class of treatment burden was identified in addition to high-increasing and low-stable classes. Although disparities in patient demographics, socio-economic status, disease count and severity, treatment burden measures, follow-up duration, etc., may exist across various studies, the available data suggested a non-monotonous trend in treatment burden over time among patients with LTCs. This may reflect the

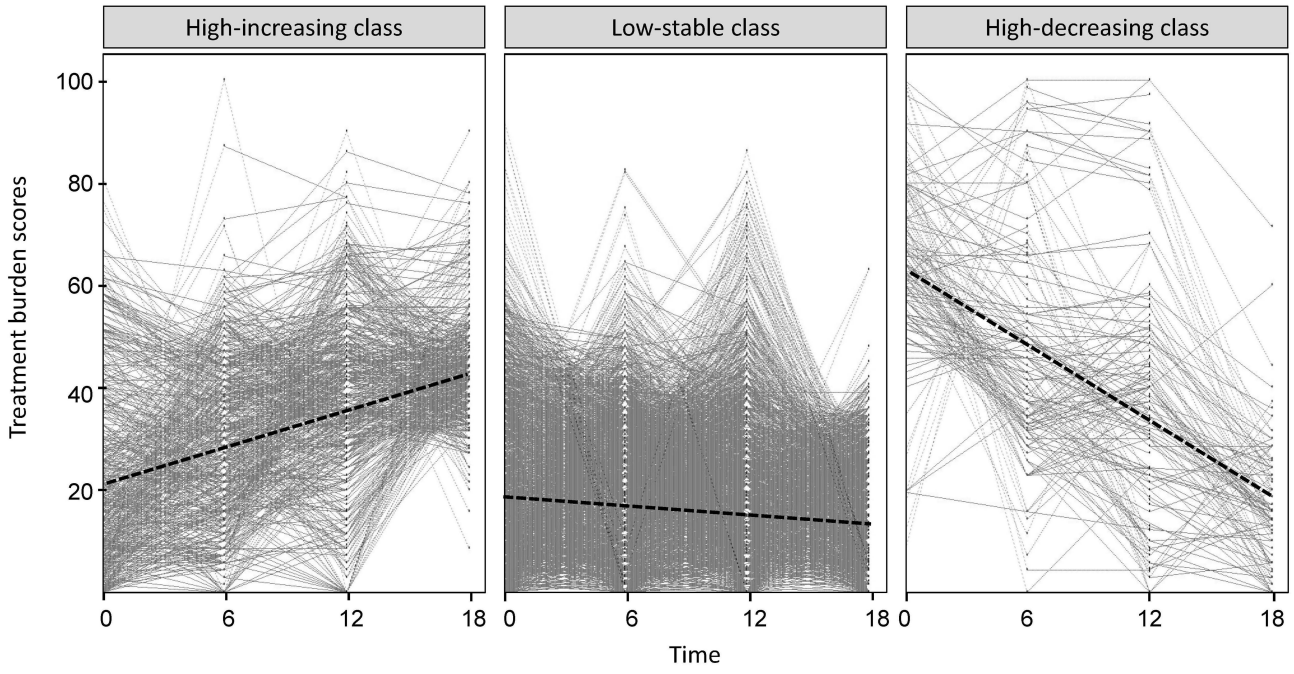


**Figure 2** Treatment burden trajectories for each of the three identified classes.

**Notes**: Individual trajectories are depicted for all members of each trajectory class, with the trend line for each trajectory class represented by a dotted black line. The X-axis represents time at each measurement point (ie, at baseline, 6, 12, and 18 months). The Y-axis represents total treatment burden scores.

**Table 3** Multivariable Logistic Regressions with Class Membership as Outcome Variable

| Patient characteristics | High-increasing *versus* Low-stable (ref.) | | High-decreasing *versus* Low-stable (ref.) | | High-increasing *versus* High-decreasing (ref.) | |
|---|---|---|---|---|---|---|
| | aOR (95% CI)[a] | *P* | aOR (95% CI)[a] | *P* | aOR (95% CI)[a] | *P* |
| Age groups, years | | | | | | |
| <60 | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| ≥60 | 1.03 (0.88–1.22) | 0.68 | 0.61 (0.44–0.84) | <0.001 | 1.70 (1.12–2.42) | <0.001 |
| Education level | | | | | | |
| College and above | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| Senior secondary school | 1.44 (1.05–1.98) | 0.02 | 0.85 (0.51–1.42) | 0.54 | 1.68 (0.94–3.00) | 0.08 |
| Junior secondary school | 1.52 (1.12–2.05) | 0.01 | 0.84 (0.52–1.36) | 0.48 | 1.70 (0.98–2.95) | 0.06 |
| Primary school or below | 1.49 (1.08–2.25) | 0.01 | 0.85 (0.51–1.43) | 0.55 | 1.47 (0.80–2.69) | 0.21 |
| Monthly household income | | | | | | |
| Less than CNY3000 | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| CNY3000 and above | 1.64 (1.23–2.18) | <0.001 | 1.33 (0.85–2.08) | 0.21 | 1.22 (0.74–2.05) | 0.43 |
| Cigarette smoking | | | | | | |
| Non-smoker | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| Smoker | 0.88 (0.70–1.11) | 0.29 | 0.88 (0.55–1.39) | 0.57 | 1.01 (0.61–1.65) | 0.98 |
| Ever-smoker | 1.24 (0.92–1.67) | 0.16 | 1.04 (0.54–1.98) | 0.90 | 1.19 (0.60–2.35) | 0.62 |
| Alcohol consumption | | | | | | |
| Non/seldom drinker | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| Regular drinker | 1.14 (0.93–1.41) | 0.19 | 0.62 (0.40–0.97) | 0.04 | 1.85 (1.15–2.98) | 0.01 |
| Ever-drinker | 1.07 (0.76–1.53) | 0.69 | 0.38 (0.15–1.00) | 0.05 | 1.19 (1.03–7.53) | 0.04 |
| Attendance in health education | | | | | | |
| No | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| Yes | 1.10 (0.92–1.33) | 0.83 | 1.72 (1.28–2.30) | <0.001 | 0.64 (0.47–0.89) | 0.01 |
| Number of LTCs | | | | | | |
| 1 | 1.00 (Ref) | | 1.00 (Ref) | | 1.00 (Ref) | |
| 2 | 1.09 (0.92–1.28) | 0.33 | 1.08 (0.81–1.47) | 0.59 | 0.99 (0.72–1.39) | 0.99 |
| 3 | 1.49 (1.21–1.86) | <0.001 | 0.93 (0.61–1.46) | 0.77 | 1.59 (0.99–2.57) | 0.06 |
| ≥4 | 1.97 (1.44–2.72) | <0.001 | 1.58 (0.87–2.85) | 0.13 | 1.25 (0.66–2.36) | 0.49 |

**Note**: [a]Models adjusted for all other independent variables.
**Abbreviations**: aOR, adjusted odds ratio; CI, confidence interval; LTCs, long-term conditions.

complexity of challenges that patients face in coping with everything they have to do to manage their health, and its impact on functioning and well-being.[5,47–49]

Existing trend analysis reported inconsistent estimates of the association between the number of LTCs and treatment burden over time. Some studies showed non-significant correlation between the number of diagnosed conditions and treatment burden scores,[14,19] whereas other studies found a moderate positive relationship.[17,18,50,51] This may be due to study differences in how diagnosed disease conditions were captured, the length of time spent living with LTCs, nature of the health system, and the availability of healthcare resources that may lessen the burden of treatment.[52] Both the main analysis and sensitivity analysis revealed that the presence of 3 or more (versus single) LTCs was independently associated with membership to the high-increasing trajectory class of treatment burden. There was, however, no evidence of a significant difference in treatment burden trajectories between patients with 2 LTCs and those with a single LTC in our study sample. We speculate that an exaggerated accumulation of individual LTC, which works with other risk factors in an additive or synergistic manner, may serve as an intrinsic part of how clustering of clinical factors complicates patient care in the course of disease and disease management. It is also worth noting that therapeutic adherence per se was not specifically assessed in the present study, and thus we were not able to determine the extent to which adherence may mediate treatment burden due to increasing numbers of LTCs. Further work is required to shed light on pathways involving incremental conditions, therapeutic adherence, and treatment burden under different clinical circumstances.

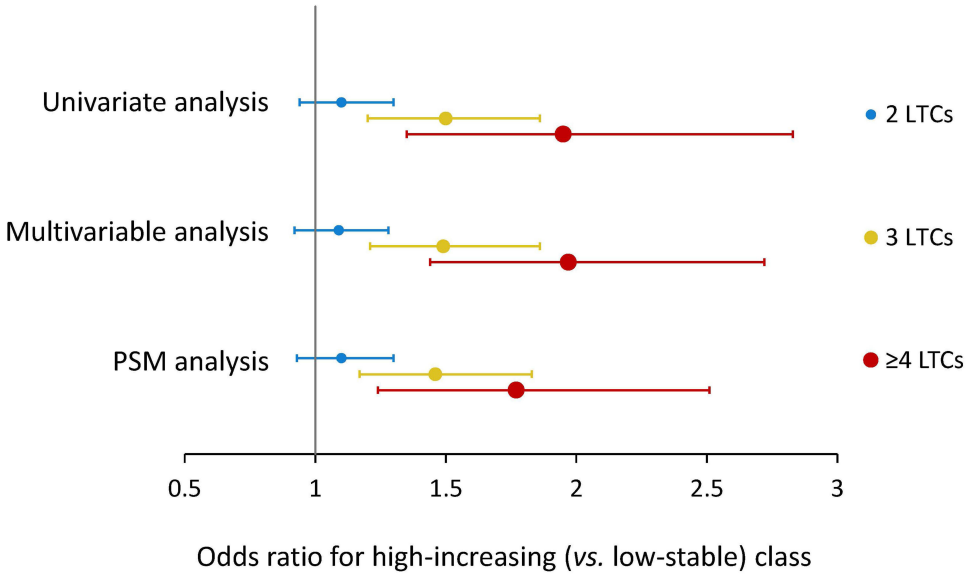


**Figure 3** Forest plot of the odds of belonging to the high-increasing (versus low-stable) class.
**Notes**: Odds of belonging to the high-increasing (versus low-stable) class for patients with the presence of 2 LTCs, 3 LTCs, or ≥4 LTCs compared to those with a single LTC were adjusted for age, education level, monthly household income per head, cigarette smoking, alcohol drinking, and attendance in health education in multivariable analysis and sensitivity analysis with the use of PSM and IPTW.
**Abbreviations**: PSM, propensity score matching; IPTW, inverse probability of treatment weighting; LTC, long-term condition; aOR, adjusted odds ratio.

Our study revealed that alcohol drinking was significantly predictive of a high-increasing (versus high-decreasing) trajectory class of treatment burden. Evidence suggests that 30–50% of people who have a drinking history may experience alcohol-use disorders including alcohol withdrawal symptoms during their lifetime, which would complicate the assessment and treatment of concurrent medical and psychiatric conditions.[53] The increased treatment burden in patients who have an intention of cessation or reduction in alcohol use may be explained by the additional "enacting work", eg, adhering to treatments and lifestyle changes, placed on patients according to the Normalisation Process Theory.[54] This fact echoes the view captured in previous qualitative studies in which lifestyle changes were considered the most difficult tasks for most patients.[5] Furthermore, we observed a significant association between attendance in health education and trajectories of treatment burden, which carries implications for health promotion and counselling strategies to promote patients' adherence to individualised plans for lifestyle modifications and therapeutic regimes in the long term. A multidisciplinary, primary care team approach with collaborative partnerships and information technology may offer substantial opportunities for a supportive environment in which skill building and coordination of care can be enhanced through joint efforts of GP clinicians, nurses, health educators, and other healthcare professionals. This may represent an important area for further investigation given the widespread transformation of primary care, particularly with respect to the delivery of equitable and sustainable care for better health outcomes.

## Strengths and Weaknesses of the Study

We examined the latent trajectory classes of treatment burden and its associated factors in a large, longitudinal, primary care sample. To our knowledge, this study offers for the first time an insight into the changing pattern of treatment burden in adult Chinese patients with LTCs over an 18-month period and provides evidence on discrete classes of treatment burden trajectories according to LCGMM analysis. The sensitivity analyses using PSM and IPTW yielded little difference in estimated associations between the number of LTCs and classes of treatment burden trajectories, suggesting the robustness of our findings. This study has several limitations. First, we cannot rule out the possibility of missed diagnosis or underdiagnosis given that we were not able to retrieve information on specialist care beyond the primary care setting. Second, a longer duration of follow-up may entail a greater risk of nonrandom participant attrition. Patients who had inadequate documentation of follow-up were excluded from the analysis, who otherwise may suffer from different organisational, personal, or financial barriers that were not captured in the present study. Third, participation in

the TBQ questionnaire survey was voluntary, and thus patients who were more satisfied with the "workload" involved in managing their LTCs may be more willing to participate in the study. This may underestimate the impact of LTCs on trajectories of treatment burden. Fourth, a patient survey restricted the inclusion of questions relating to physician information, eg, training and qualifications, and years of practice, which was not accounted for in this study. Last but not least, study participants were drawn from government-owned and hospital-managed CHCs. The generalisability of our findings to other primary care populations should be interpreted with caution.

## Conclusion

Our study revealed the presence of discrete patterns of patient-level treatment burden in primary care patients living with LTCs. Three trajectories of treatment burden, ie, high-increasing, low-stable, and high-decreasing, were identified via LCGMM. The data supported a non-monotonous trend in treatment burden over time, providing directions for tailored interventions to optimise disease management. Patients with 3 or more LTCs should receive close attention in the delivery of care as they tend to experience a greater treatment burden.

## Data Sharing Statement

The datasets used and analysed during the current study are available from the last corresponding author (HHXW) upon reasonable request.

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## Disclosure

The authors declare that there are no conflicts of interest in this work.

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