Original Article

Relationship between Health Behavior and Metabolic Syndrome Progression: The Parallel Latent Growth Curve Model

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Abstract

OBJECTIVES: This research aims to develop a measurement model to assess a relationship between Metabolic Syndrome (MetS) progression and health behavior changes.

MATERIALS AND METHODS: Medical records of selected patients attending checkup clinics of a private hospital from 2006-2017 were reviewed. Clinical and questionnaire data that assessed exercise (EXE), smoking (SMK), and failure to control weight (FCW) including waist circumference (WC) and body mass index (BMI) as well as laboratory results (i.e., blood pressure (BP), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides (TG), and fasting blood sugar (FBS) were retrieved. The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) was applied to diagnose MetS and a parallel latent growth curve (LGC) model was used to assess relationships between health-related behaviors and MetS progression. Analysis of Covariate (ANCOVA) were used to determine the influence of sex and age as co-variates of the model.

RESULTS: Among 1,296 patients, 61 (4.7%), 64 (4.9%), 70 (5.4%), 73 (5.6%) and 87 (6.7%) patients had MetS each year. The FCW had strong effects on the initial prevalence (coefficient 0.69) and trend (0.57) of MetS progression while EXE had small negative (-0.05 and -0.07) and SMK had small and positive (0.01 and 0.03) effects. Age and gender contributed to MetS indirectly through FCW. Decomposition of effects revealed high relationship between FCW and the initial prevalence (0.69) and trend (0.57) of MetS. The SMK had indirect effect on TG (0.66) and HDL (-0.61) but these effects were diluted off after controlled for effects of other variables. **CONCLUSION:** We have brought to light the hidden (latent) aspect that age and sex result in MetS through FCW. With the significance of FCW, which subsequently increases risks for several NCDs, healthy eating should be the most important health promotion topic to avoid MetS progression. The LGC model can be used to supplement the diagnostic and prognostic scores for both physicians and health teams because it provides more detailed information of hidden (latent) relationships. Mobile phone applications using this model should be developed in order to promote self-regulation among MetS patients. Future research should be conducted for revision, calibration and validation of the NCEP ATP III criteria and the current research risk scores.

Keywords: Metabolic Syndrome, latent growth curve, weight, control, smoking, exercise

Metabolic Syndrome (MetS) is a constellation of clinical
manifestations of metabolism abnormalities of high BP, high
helly fat or central obesity. These fats cause persistent inflammatory manifestations of metabolism abnormalities of high BP, high TG, FBS and lower HDL level along with the symptom of belly fat or central obesity. These fats cause persistent inflammatory reaction, hormonal imbalance, and insulin resistance syndrome which leads to diabetes mellitus type 2, and cardiovascular diseases.¹⁻³ The people with MetS are also at greater risk of having other non-communicable diseases (NCDs).

NCDs are leading causes of death worldwide (82 % of total death). One-third of those are heart diseases and vascular diseases, which is 37%. In which, 17 million are under the age of 70.4 According to the World Health Organization, in 2014 there were approximately 422 million people living with diabetes mellitus (DM) worldwide. Without prevention plans, at least 629 million cases are expected by 2045. The patients with DM increase significantly in low- and middle-income countries, and younger age groups.⁵ The prevalence of high BP, also called a 'silent killer', as patients may not show symptoms. For the past 40 years (1975-2015), number of people with high BP increased from 594 million to 1.13 billion in 2015, especially in low- and middle-income countries.6 It results in more than 50,000 deaths among Thai people each year.7

As a significant risk for chronic diseases, MetS is a public health concern worldwide. It causes negative impacts on economy and society thus hinders country development. To prevent MetS, promotion of health-related behaviors focusing on weight control and physical activities are promoted.⁸⁻¹⁰ Reduction of other risk factors are also encouraged such as SMK behavior cessation, limiting alcohol consumption, reduction of high fat consumption and having enough sleep.¹¹

This study examines the relationship between healthrelated behaviors and MetS. The model had been developed based on conceptual framework that there are two groups of health-related behaviors that are associated with MetS. The first group includes health behaviors that promote MetS such as ignorance to control weight, regular SMK behavior and unhealthy diets. The second group includes behaviors that reduce or slow down disease progression such as healthy diets and physical EXE. From annual check-ups data, in particular laboratory results, patients who had at least three of five criteria defined by The NCEP ATP III were diagnosed as having MetS. The five criteria^{12,13} are:

- 1. Abnormal Waist Circumference (WC) (male ≥ 90 centimeters (cm) and female ≥ 80 cm),
- 2. FBS ≥ 100 mg/dl or diagnosed with DM
- 3. TG level > 150 mg/dl.
- 4. Serum HDL cholesterol ≤ 40 mg/dl. in male or ≤ 50 mg/dl in female
- 5. $BP \ge 130/85$ mmHg or receiving medicine for hypertension

The technique used in analysis is the parallel LGC model.

Materials and Methods

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This study is a retrospective chart review of longitudinal data. Study protocol was approved by the Board (Protocol Approval number BMC IRB 2018-06-026). Data used in this research were from annual check-ups collected from unidentified patients of a large private hospital from 2006 to 2017. Selection criteria were

1. Age \geq 18 to 65 years old

- 2. Thai nationality
- 3. All variables in this model must complete in each year and had five years of consecutive annual check-ups, each record must have full set of required variables.

Data were analyzed using R code with lavaan (latent variable analysis) version 0.6-1 package.

The study looks at the same phenomenon at different time points focusing on changing progress of the characteristics or conditions of the phenomenon. Same variables are repeatedly measured in different time periods 14 to observe a result caused by a particular factor more clearly and more precisely according to the Cause and Consequences principle.

Structural Equation Modeling (SEM) is a statistical analysis technique that aims to study a model of causal relationship between theoretical latent variables (or constructs) and many variables, either between exogenous variable and endogenous variable or between latent variables and observed variables through estimation of several parameters of the model at the same time. Generally, it is to verify the accuracy of models created from literature review, concepts, theories and supporting research, when compared with empirical data. Importantly, SEM analysis is flexible for preliminary agreement by allowing the error of data obtained from measurement of each observed variable to be related, this makes the results from SEM be more accurate.¹⁵

LGC is one form of SEM that focuses on a trajectory to examine longitudinal change over time and to examine intra-individual changes as well as inter-individual differences in intra-individual change.¹⁶ The change can be positive or negative while the shape of a change can be linear or nonlinear growth patterns.17 LGC relies on the concept that each measurement consists of composite scores of three parts, namely intercept, slope and error. Firstly, intercept (I) is the value of the outcome when the growth curve begins. It remains constant for any individual across time (i.e., initial level). The intercept is the value of the outcome when the growth curve begins. Secondly, the slope (S) of an individual's marital discord trajectory represents the rate of change in the outcome over time (i.e., rate of change). Thirdly, an error (e) is associated with observed variables that represent measurement error. LGC technique is very useful for analyzing longitudinal data, with the ability to generate graphs that show a pattern of change over time.18

Parallel LGC is an advanced version with two parallel models for two variables. This version of LGC is used when simultaneous trajectory change is required. The technique allows researchers to build a model for multiple growth processes simultaneously to assess an initial score and slope for more than 2 points to test hypotheses about interrelationships.19 The slope of this model, rate of change of factor can change an initial value of first measurement of another factor.

In this study, the LGC model was constructed with an assumption that MetS is resulted from poor health-related behaviors. Therefore, we focused on the three health-related behaviors of

- 1. FCW is defined by 2 factors, WC and BMI, which are indicators of MetS
- 2. Smoking behavior (SMK).
- 3. Extent of exercise behavior (EXE).

While we used data from check-up questionnaires available in the medical record to classify subjects on their SMK and EXE condition, FCW was classified using BMI and WC. The MetS status was determined according to the NCEP ATPIII criteria. Laboratory results from 5-year annual health check-ups were extracted for this. They were FBS, TG level, HDL level, LDL level, and high BP (systolic BP (SBP) >130 mmHg or diastolic BP (DBP) > 85 mmHg), The slope was 0, 1, 2, 3, 4 for the years 1, 2, 3, 4, and 5 respectively. All variables have a default Intercept (Intercept, I) as 1 in every measurement (every year).

 Figure 1: Parallel Latent Growth Curve (Baseline Model)

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After data were extracted, transferred and prepared, descriptive statistics for baseline characteristics of the study sample were calculated. A parallel LGC was employed to examine the longitudinal trajectories of MetS progression and its relationship with health-related behaviors as well as laboratory results over the duration of five years. An analysis of covariance (ANCOVA) was also conducted to include gender and age to assess their effects on the relationship between health-related behaviors and MetS progression.

A model was constructed to include Covariance between variables as follows, SEXE and IEXE, SEXE and SSMK, IEXE and SSMK, SSMK and ISMK, ISMK and IFCW, SFCW and IFCW, SMK_4 and SMK_5, WC_2 and BMI_2, WC_3 and BMI_3, SBP_1 and DBP_1, SBP_2 and DBP_2, SBP_3 and DBP 3, the last pair are SBP 4 and DBP 4.

In Figure 2, latent variables are labelled ovals while observable variables are labelled in rectangles. Latent variables are "not observable" because they play roles in the model. On the contrary, observable variables are measurable as we can quantify or classify them among our subjects.

Latent variables in our model are intercepts and slopes of EXE, SMK, FCW, SBP, DBP, HDL, LDL, TG and FBS. There are two types of latent variables, external and internal ones. While health-related behaviors namely EXE, SMK, and FCW were considered as external factors, clinical and laboratory findings were considered as internal factors. These internal factors included BP (SBP, DPB), HDL, LDL, TG and FBS. WC and BMI were considered as surrogates of FCW; thus they were part of external factors.

Relationship or effects between two variables are categorized into direct and indirect effects. Direct effects are those one on one between health-related behaviors and MetS (i.e., EXE on MetS, SMK on MetS and FCW on MetS). Indirect effects are those via a mediator (e.g., EXE on TG on MetS). Summation of direct and indirect effects results in Total effects.

We also looked at standardized and unstandardized estimates of these effects. Standardized estimates are level of variation of all independent variables on the dependent variables (MetS) while unstandardized estimates take into account only the variation of an independent on the MetS. Standardized estimates are preferred as they result from more "controlled" calculation.

The model goodness-of-fit of each LGC was evaluated based on a relative chi-square, which is the chi-square $(\chi 2)$ index divided by the degrees of freedom (df). This index might be less sensitive to sample size. The criterion is ranging from less than 2 to less than 4.20-22 The comparative fit index (CFI) measures the relative improvement in fit going from the baseline model to the postulated model.23 Tucker–Lewis index (TLI) measures a relative reduction in misfit per degree of

freedom.24 CFI and TLI values of 1 indicate a perfect fit and cut-off point values \geq 0.95 are indicative of a good fit. The Root Mean Square Error of Approximation (RMSEA) is a badness-of-fit measurement, yielding lower values for a better fit. The goodness of fit index (GFI) is the proportion of variance accounted for by the estimated population covariance cut-off point of values greater than 0.90 has been recommended.²⁵ An RMSEA \leq 0.06 could be considered acceptable.26 Standardized Root Mean Square Residual (SRMR) is an index of the average of standardized residuals between the observed and the hypothesized covariance matrices a value less than 0.08 is generally considered a good fit.26,27

Results

From 26,172 patients, only 1,295 had complete health records and met the inclusion criteria, and 43.3% were male and 56.7% were female. Average age was 46.4 ± 10 years among male and 47.2 ± 9 among female subjects. Looking at age distribution, the majority were in middle age and older groups. According to the NCEP ATP III criteria, five variables are used for the diagnosis of MetS. They are FBS, WC, HDL, TG, and BP (systolic and diastolic). Male had higher average values of those items than female subjects, except HDL, in that the average value for female subjects was higher than for male subjects.

Additional variables related to MetS status beside the NCEP ATP III criteria that we collected were BMI, total cholesterol, and LDL. More than half (57.6%) of female subjects had normal BMI while only a quarter (25.0%) of male had normal BMI and the majority (73.6%)of male subjects were overweight or obese. Regarding total cholesterol, a little below half of female (46.0%) and male (43.9%) subjects were in normal range. Around half of female subjects (47.1%) were in the high LDL group while more than half of male subjects (64.3%) were in this category.

For health-related behaviors, both female and male subjects had similar pattern of EXE (57.7% to 58.8% EXE sometimes) but not SMK. Greater proportion of male subjects reported current smokers (12.1%) or ex-smokers (11.6%) while a smaller proportion (1.5%) of female subjects reported so (1.5% current, 1.2% ex-smoker).

The proportion of MetS, according to NCEP ATPIII criteria, was higher (7.3%) among male than female (2.7%) subjects. When analyzed data according to NCEP ATP III criteria by year, as in Table 2, the number of patients with MetS was increasing each year.

The Parallel LGC model was constructed and model outputs are shown in Figure 2. The statistical values for consistency check of the model goodness-of-fit were evaluated using as follows:

 χ 2/df = 3.5, CFI = 0.97, TLI = 0.97, GFI = 0.89, SRMR = 0.05, $RMSEA = 0.04$.

Table 2: Proportion of Metabolic Syndrome (MetS) by year, according to NCEP ATP III criteria.

All four of those values passed criteria except GFI value ((.89), which was affected by sample size.30, 31 The overall, this model is consistent with empirical data. Analysis of Covariance (ANCOVA) was conducted to assess significance of age and gender on the intercept and slope of MetS.

As shown in Table 3, Analysis of Covariance (ANCOVA) of intercept value shows that gender has a significance level of 0.560 and age has a significance level of 0.881. So, age and gender do not have significant effect on the intercept of MetS (i.e., no significant effect on initial prevalence of health behavior and MetS progression). From Table 4, a significant level of gender is 0.717 and that of age is 0.831 (i.e., no significant effect on progression to health behavior and MetS).

These findings demonstrate clearly that among our subjects, during the 5-year follow up period age and sex did not have significant effects on both the initial prevalence and subsequent trends of MetS.

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 Figure 2: Parallel Latent Growth Curve (Standardized)

Table 3: Analysis of Covariance (ANCOVA): **Intercept** of variables affecting metabolic syndrome

To explore effects of EXE and SMK on the initial prevalence and subsequent trends of MetS, we look at slopes and intercept relationships in terms of correlation coefficients as follows.

- 1. Relationship between intercept and slopes of EXE and MetS appeared to be -0.05 (IEXE \rightarrow IMetS) and -0.07 $(SEXE \rightarrow SMetS)$, both values were negative. The interpretation is that EXE was a protective factor for both the initial prevalence IMetS and trend of SMetS. Subjects with more EXE started with lower rate of MetS (initial prevalence or intercept) and as time passed by, their likelihood (lower trend or slope) to progress to MetS compared with those who had lower level of EXE behavior. However, degree of relationship is small.
- 2. Relationship between intercept and slops of SMK and MetS was found to be 0.01 (ISMK \rightarrow IMetS), and 0.03 (SSMK \rightarrow SMetS), both values were positive. This means, SMK behavior was a risk factor for the initial prevalence IMetS and trend of SMetS. The greater level of SMK behavior, the greater risk to have MetS. Subjects who had SMK behavior started with a little higher rate of MetS and as time passes by, they were more likely to progress to MetS compared with those who did not smoke cigarettes. Also, the degree of relationship was small.
- 3. Finally, the relationship between FCW and MetS in terms of intercept and slope appeared to be 0.69 (IFCW \rightarrow IMetS), and 0.57 (SFCW \rightarrow SMetS), both values were positive with rather high values. These indicated that FCW (or eating habit) had greater effect on progressing to have MetS than EXE or SMK behavior. Subjects who could not control weight were at moderately higher rate of MetS at the initial stage and as time passes by they were more and more likely to progress to MetS.

WC and BMI were included in the model as FCW indication. Relationship between SWC and SFCW was found to be 0.97, while SBMI and SFCW was found to be 0.81. In terms of intercept, relationship between IWC and IMetS was found to be 1.00, while that IBMI and IMetS was 0.90. Altogether, these means WC had greater effect than BMI did on FCW. However, both were used for FCW assessment. If both WC and BMI were high FCW would be more likely, which subsequently resulted in greater chance of MetS as demonstrated in number 3 above.

In terms of errors (e), we found quite small values of them Errors of EXE behavior (e1, e2, e3, e4, e5) in each year was 0.01, 0.08, 0.09, 0.08 and 0.01 while errors of SMK behavior (e6, e7, e8, e9, e10) were 0.01, 0.05, 0.04, 0.02 and 0.05 for the same duration. The same magnitude of errors was also found for WC (e11, e12, e13, e14, e15) at 0.02, 0.03, 0.02, 0.02 and 0.08 and of BMI (e16, e17, e18, e19, e20) were 0.01, 0.05, 0.04, 0.02 and 0.05. All of these indicate that health-related behaviors were quite stable, or, simply speaking, not easy to change during the follow-up time period of five years. In addition, small magnitude of errors indicates high accuracy of predicting observable variable by hidden variables. We can say that our model has high level of accuracy.

Loading values reflect association between observable and latent variables. It ranges from 0.0 to 1.0. A higher loading value indicates "stronger" association.

In this group of subjects, we found loading values of health-related behaviors, i.e., EXE and SMK behavior and failure to controlled weight remained high. The loading value of Slope and loading value of Intercept in each year appeared to have the same pattern. This reflects that there was little to no change in the health-related behaviors of subjects. For example, in the first year, subjects started with no EXE, in the subsequent years, they continued with no EXE. Similarly, subjects with the first year of SMK behavior remained SMK behavior in subsequent years. High loading values point out to the same interpretation that changing health-related behaviors was difficult, as for many people, poor health-related behaviors could have been "habitual".

Among all five laboratory results, the highest intercept value was TG (ITG and IMetS) 0.76, followed by IHDL and IMetS was -0.74 (negative value), IBP and IMetS was 0.63 (positive value), IFBS and IMetS was 0.57 (positive value), ILDL and IMetS was 0.31 (positive value). The higher value of Intercept indicated greater influence on progressing towards MetS. This set of findings indicated that TG had the highest effect, followed by (systolic and diastolic), then FBS and LDL. Simply speaking, subjects with higher TG or BP were at a greater risk "at the initial stage" to have MetS than those who had lower levels of these. On the contrary, those with higher HDL level were at a lower risk "at the initial stage", as the HDL has negative relationship value indicating its preventive factor in nature.

Our model had STG and SMetS of 0.84, followed by SHDL and SMets was -0.82, SFBS and SMets was 0.46, SLDL and SMets was 0.33, and lastly SBP and SMets was 0.22. These indicated that triglyceride had the highest effect on trends towards having MetS, followed by FBS, LDL and blood sugar respectively. On the contrary, HDL was a preventive factor, which reduced trends of MetS development. This means subjects with high TG would have greater trend to turn to MetS as time passed by. HDL showed protective effects as it was related with decreasing trend.

Altogether a person with high level of TG needs to change her/his diet to reduce TG level to normal. Oppositely, if s/he has lower HDL than the standard scale, she/he should increase the HDL level in order to avoid MetS.

Viewing health-related behaviors (i.e., EXE, SMK, and FCW), as external factors. The remaining clinical and laboratory findings (BP, HDL, LDL, TG, FBS and MetS) could be viewed as internal factors. Outputs of the model allowed us to explore relationships between these external and internal factors. The model gave us the "decomposition" of relationships because both direct and indirect relationships among these factors were calculated. Standardized and unstandardized correlation

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coefficients between intercepts and slopes of relevant variables were calculated and displayed in Tables 5 and 6.

Table 5 focuses on the intercepts, thus showing relationships between relevant variables at the initial stage. Relationship between FCW and MetS was at 0.69 showing rather high effects of FCW on prevalence of MetS than the higher degree of FCW, related with higher prevalence of MetS. FCW also had moderately negative (-0.51) relationship with HDL, moderately positive (0.52) relationship with TG, moderately positive relationship (0.43) with BP and low level of relationship with LDL (0.21) and FBS (0.39).

It is worth noting that SMK and EXE had little relationship (effect) on prevalence of MetS as their correlation coefficients ranged from 0.02 to 0.10. The same level of relationship is found between SMK, EXE and BP, HDL, LDL, TG and FBS.

We may conclude that prevalence of MetS (at the beginning of follow up) results mostly from FCW with little effects from EXE and SMK behaviors.

Table 6 shows the same pattern of relationship between FCW and MetS, with an additional finding of unstandardized relationship between SMK and HDL and TG. Increasing trend (slope) of FCW is related with increasing trend (slope) of MetS meaning that during the follow up period, increasing trend of FCW resulted in increasing trend of MetS (0.57). Similarly, increasing trend of FCW resulted in decreasing trend of HDL (-0.47), increasing trend of TG (0.48) with moderate to low effects on BP (0.13), LDL (0.19) and FBS (0.26). The model found high relationship (effect) of increasing trend of SMK on decreasing trend of HDL (-0.61) and increasing trend of TG (0.66). However, this high relationship was unstandardized, meaning not controlled for effects of other variables as the standardized ones fell to low level of relationship.

Table 5: Decomposition of the level or status (intercept) of endogenous variable (Intercepts) (Numbers in the table are correlation coefficients. Higher values indicate higher effects)

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Table 6: Decompositions for Effects of trends (slope) of exogenous variable on the trends (slope) of endogenous variables

Discussion

Our study has brought to light the hidden (latent) aspect of how older age and male gender results in high prevalence and trend of MetS. In addition to the consistent observation that older age and male gender are two determinants of MetS, our study has demonstrated that age and sex has an indirect relationship with MetS through the situation of FCW. This hidden (latent) aspect of relationship was identified through using relevant statistical analysis and fitting a Parallel LGC model.

Our finding corroborates with those of Park YW32 that the main cause of MetS is weight gain. In that study, FCW affects TG and HDL. Gaining weight increases TG and greatly reduces HDL. Higher TG level is the result of poor eating habits or having diets with high fat, high carbohydrate, high sugar or high alcohol. It has been documented those high TG level causes obesity.33

Many literatures confirm that SMK behavior and lack of EXE lead to MetS.^{32,34} However, in our model, the scale of effect of both variables are small. This might be from data

quality. These data were collected through surveys and subjected to some information and recall biases of subjects. In addition, the effects of BP, LDL and FBS on development of MetS are also smaller than those that appear in the literatures. Again, this might be from the conditions of medical records of private hospitals, where history of some medication could be missing.

The strength of this study is that behavioral data were collected from patients of middle to high education and socio-economic communities. Health checkup data of five consecutive years allowed us to assess progress of healthrelated behaviors that could affect the disease, as well as progress towards MetS at high accuracy level.

Before generalizing our findings, we acknowledge that our subject group was not a representative sample of Thai population. As described, we used data of patients who attended check-up clinics of a private hospital. Our subjects were from middle to high socio-economic status. The majority of them received company benefits, welfare and had

health insurance. According to Thailand National Statistical Office, those samples account for only 9% of the Thai population. In addition, medical records for conditions associated with MetS such as high BP, hyperlipidemia, and DM could appear in several locations in the medical record system and we might not have covered them all. This may result in selection bias thus affecting accuracy of the model.

Findings from this study could supplement revision of NCEP ATP III criteria, and if required to relevant clinical guidelines. Increased sensitivity or early diagnosis of MetS would contribute to early warning for patients with a risk of MetS so that they can incorporate healthy behaviors earlier in their lives. Most significantly, our study has demonstrated that MetS is the outcome of modifiable health-related behaviors that are easy to monitor, FCW. It is not from genetics or old age.

Conclusions

Data of 1,296 patients who attended five consecutive annual checkups in a private hospital in Thailand were included in this study to assess the relationship between health-

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related behaviors and MetS using a parallel LGC model. Among our subjects, FCW had significant effects on prevalence and trend of MetS both directly and partly through TG and HDL levels.

Conflict of Interest

The authors declare on conflict of interest.

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