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Healthcare Cost Trajectories in the Last 2 Years of Life Among Patients With a Solid Metastatic Cancer: A Prospective Cohort Study

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eAppendix 1. Singapore's Healthcare Financing

Singapore's healthcare financing is based on "3 M's": MediSave, MediShield Life, and MediFund.[1–4]

MediSave is national medical health savings account to help cover out-of-pocket payments for medical bills for self and family members. MediSave can be used to pay for a broad range of outpatient treatments, hospitalization, and day surgery expenses as well as premiums for MediShield Life.[5] Personal and employer salary contributions (8%–10.5%, depending on age) to MediSave accounts are compulsory for all working citizens and permanent residents. There are limits on withdrawals from MediSave.

MediShield Life is a universal basic public health insurance with high deductibles. It is mandatory for citizens and permanent residents and covers some part of large hospital bills and select costly outpatient treatments, such as chemotherapy and radiotherapy.[5] It is structured such that patients pay less using MediSave/cash for large hospital bills for receiving subsidized treatments (B2/C-type hospital wards) in public hospitals. In Singapore, approximately two-thirds of patients opt for such subsidized treatments.[6] The maximum amount that can be claimed from MediShield Life varies by treatment type and length of hospital stay. The maximum claim limit per policy year is set at SGD $100,000 (USD $71,837).[5] There is no lifetime limit.

MediFund is the government's safety net for needy Singaporeans who cannot cover their out-of-pocket health expenses after using MediShield Life and MediSave.

Private Health Insurance

Individuals who wish to obtain additional healthcare coverage for private hospitals or want to be cared for in private wards in public hospitals can opt for an Integrated Shield Plan, which combines MediShield Life with additional private health insurance.[6] Integrated Shield Plans ride on MediShield Life and are available only to citizens and permanents residents who can pay the premium using their MediSave account. There are also other private health insurance options offered by for-profit insurers that are not integrated with MediShield Life. Premiums for these other insurance options cannot be paid from MediSave. In our sample, approximately 62% of patients had some form of private health insurance.

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eAppendix 2. Group-Based Trajectory Modeling

Why Group-Based Trajectory Modeling?

In medical sciences and in clinical and developmental psychology, researchers are interested in modeling developmental trajectories or patterns of change in an outcome across multiple time points. For example, medical researchers may be interested in studying the progression of a disease over time. A common approach to study such developmental trajectories is to use standard growth analysis (growth curve modeling) that estimates a single trajectory that averages the individual trajectories of all members of a given sample.[1] In statistical terms, a standard growth analysis estimates 1 average intercept and 1 average slope for the outcome variable with time as the independent variable. Individual variation is captured by estimating a random coefficient. This approach may be useful if we assume that the pattern of change in the outcome for all members of the sample is similar.

However, in the real world, the pattern of change for most outcomes varies between individuals. Many researchers thus divide the sample using observable criteria (eg, men and women) or subjective criteria (eg, by using different thresholds for cost) and construct separate trajectories for each subgroup. One limitation of this approach is that these subgroups need to be identified ex ante. In contrast, group-based trajectory modeling (GBTM) is a statistical methodology for analyzing developmental trajectories that are not identifiable ex ante based on some observable individual criteria.

Technique and Assumptions

GBTM is a semiparametric technique based on finite mixture modeling that identifies distinct subgroups of individuals following a similar pattern of change over time for a given outcome.[1–4] Unlike growth models in which individual differences are captured by random coefficients, individual differences in GBTM are captured by a finite set of unique polynomial functions, each corresponding to a discrete trajectory. In other words, instead of 1 slope and 1 intercept, GBTM estimates j intercepts and j slopes, assuming there are j trajectories. However, within a trajectory, the slope and intercept are not assumed to vary across individuals. This assumption can be justified because the individual differences are mostly captured by the multiple trajectories. The way the outcome of interest has been measured or defined dictates the specific probability distribution used to estimate the parameters. Currently, GBTM analysis in SAS/STATA allows censored normal, binary logit, Poisson, and β-distributions for the outcome.

For a censored normal model, each trajectory is described as a latent variable (y_{it}^{*}) for a given trajectory (j) at a specific time (t) as follows[5]:

$$y_{it}^{*} = \beta_0^j + \beta_1^j X_{it} + \beta_2^j X_{it}^2 + \beta_3^j X_{it}^3 + \varepsilon_{it}$$

In the equation, X represents the independent variable (time/age). The trajectories can be modeled as a polynomial of any order. In the above equation, for example, each trajectory is modeled as a cubic function. The coefficients of the polynomial terms dictate the shape of the trajectories.

Estimation

To estimate the model, the researcher has to specify the number of trajectories to be extracted from the data. Next, for the number of trajectories specified, the researcher should specify the polynomial function for each trajectory. Preferably, this should come from theory. In the absence of theory, to identify the optimal number of trajectories and the polynomial function defining each trajectory, we first fitted models with one trajectory and sequentially increased the number of trajectories. For each specified number of trajectories, we started with a quintic polynomial function and moved down by an order of 1 if the specified function was not statistically significant. We retained the highest-order model that was significant. We considered the Bayesian information criterion, the value of trajectory membership probability (≥5%), the odds of correct classification (≥5), and the average posterior probability (≥0.7) to choose the optimal number of trajectories, aiming for parsimony in the number of trajectories.[1]

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eAppendix 2. Group-Based Trajectory Modeling (cont.)

The model is estimated in STATA, version 16.0 (StataCorp LLC) using the following command[6]:

traj, var (dependent variable*) indep(independent variable*) model(cnorm)

order (5 5 5 4) max(13) min(0) risk(other independent variables) refgroup (3)

In our analysis, log-transformed bimonthly total healthcare cost is the dependent variable and months before death is the independent variable. "cnorm" specifies that a censored normal distribution is used to estimate the parameters. The order specifies the polynomial function for each trajectory. After the iteration technique detailed above, we used a quintic function for the first 3 trajectories and a quartic function for the last trajectory. The maximum and minimum values are observed maximum and minimum values of the dependent variable in the sample. After the optimal model is obtained using only time as the independent variable, we introduce more independent variables in the option "risk" to estimate how these variables impact the membership in each trajectory. "refgroup" specifies which of the trajectory groups should be used as a reference group while presenting the results.

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