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Gompertz Distribution for Survival of Inpatients with Cluster Comorbidities

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Abstract

Cluster comorbidity explains statistically significant associations between diseases without etiological explanation. Our prior study shown that multimorbidity can be separated into three clinically consistent clusters, namely gastrointestinal low back pain and anxiety disorders (GLAD), cardio-metabolic and pain disorders (CMPD), and cardio-pulmonary disorders (CPD). The aim of this study is to assess the extent at which each cluster influences the survival of elderly patients. The study utilized follow-up clinical data of 154 inpatients in the age group 50+ from a health facility in Ghana. The dataset was computationally formatted as right censored from which the Gompertz survival model was fitted. Overall, 61 mortalities were observed, of which 52.5%, 32.7% and 14.8% were patients with diseases classified under CMPD, CPD and GLAD respectively. We demonstrated that the pattern of survivorship of these patients is Gompertz distributed. As per our model, we found that the risk for mortality associated with the comorbidity clusters increases exponentially over the length of hospital stay. The patients with diseases classified under CPD and CMPD have increased risk for mortality with hazard ratio (HR) of 3.85 and 3.76 respectively, compared to GLAD with HR of 1.0.

Keywords: Gompertz Distribution; Hazard Function; Cluster Comorbidity; Multimorbidity Pattern

1. Introduction

Survival models have gained popularity in medical literature for the task of analysing time to event data. In survival studies, time generally represent years, months, weeks, or days from the beginning of follow-up of an individual until an event occurs. Alternatively, time can refer to the age of an individual when an event occurs. However, event means death, disease incidence, relapse from remission, recovery or any designated experience of interest that may happen to an individual [7]. On some occasions time to event data follows a predictable pattern. In this situation survival models with parametric distributions such as Exponential, Weibull, Gompertz and Gamma can be used to describe time to event. Most interesting survival models examine the relationship between survival and one or more predictors, usually termed covariates. In medical research, the Cox proportional hazards model is widely employed within this context compared to parametric models. However, in one study a class of parametric

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models, i.e. Weibull and Exponential models were found to be more consistent with data than the Cox model when analyzing survival time of patients with stomach cancer [8]. Moreover, a recent comparison in a study by [11] yielded similar results. The Gompertz distribution provides a convenient way of describing survival in human subjects and it is frequently used to describe the distribution of adult deaths.

The extraction of common chronic diseases that are significantly associated (i.e. cluster comorbidities) from those co-occurring by chance in a given population, particularly the aged has been the focus of many recent multimorbidity studies [12, 6, 4, 10]. This research approach has led to discoveries of a variety of common cluster comorbidities or multimorbidity patterns from different populations. It has been argued that further studies should focus on the impact of different multimorbidity patterns on mortality, disability, quality of life and many other health outcomes. The existing studies of this subject are largely configured to general multimorbity [3, 2, 5, 1]. To the best of our knowledge only one study has prepared the analysis from the perspective of diseases with clinically consistent patterns that pertain to multimorbidity [9].

It is in this path that this paper is organised to clarify how different comorbidity clusters or multimorbidity patterns influences the survival of patients within the context of Gompertz distribution. Specifically, this research utilised the multimorbidity patterns of gastrointestinal low back pain and anxiety disorders (GLAD), cardio-metabolic and pain disorders (CMPD), and cardio-pulmonary disorders (CPD) from a prior study [9], by studying their impact on the length of stay until death of elderly patients with two or more diseases within any of the clusters in the inpatient units of the Kwadaso S.D.A hospital in Kumasi, Ghana.

2. Method

The basis of statistical analysis of this study is based on inpatient follow-up data maintained at Kwadaso S.D.A hospital in Kumasi, Ghana. The dataset relates to 154 in-patients of age 50 and above diagnosed with two or more chronic diseases in any of the following multimorbidity patterns: GLAD (gastritis, peptic ulcer disease, anxiety, low back pain), CMPD (arthritis, diabetes mellitus, migraine, hypertension) and CPD (asthma, congestive heart failure, stroke) [9] from October, 2011 to July, 2012. Medical information on morbidity status, health outcome (i.e. mortality or discharge) and length of hospital stay (in days) were retrieved for all patients (both male and female).

Using the length of hospital stay until death as survival time the data was organized as a survival object by treating unknown survival time (i.e. those discharged and those surviving past the end of study) as right censored. The Gompertz model was then fitted by using survival time as the response variable and the multimorbidity patterns as covariate. The risk for mortality associated with the multimorbidity patterns was specified by the Gompertz hazard function.

$$\theta(t,X) = \lambda exp(\gamma t) \tag{1}$$

by reparameterizing the parameter λ in terms of the covariate and Gompertz regression coefficients. This was expressed as

$$h(t) = [exp(\gamma t)]\, exp(\beta_0 + \beta_1 X_1 + \beta_2 X_2) \tag{2}$$

where $h_0(t) = [exp(\gamma t)]$ is the baseline hazard which is parametrically specified. The $\beta's$ are the Gompertz regression coefficients, γ is the shape parameter and t represents time. The X_1 and X_2 corresponds to the categories of the covariate vector X with the base category corresponding to β_0. If $\gamma > 0$ then the hazard exponentially increases over time. On the other hand, if $\gamma < 0$ then the hazard decreases exponentially over time and if $\gamma = 0$ then the hazard is constant and reduces to the exponential model. The measure of effect was typically obtained by

the hazard ratio (HR) which is defined by

$$HR = exp(\beta) \tag{3}$$

Moreover, the survivor function which takes the form

$$s(t) = exp\left[-\frac{\lambda}{\gamma}(exp(\gamma t) - 1)\right] \tag{4}$$

was expressed in terms of the coefficients as

$$s(t) = exp\left[-\frac{exp(\beta_0 + \beta_1 X_1 + \beta_2 X_2)}{\gamma}(exp(\gamma t) - 1)\right] \tag{5}$$

These analyses were computationally implemented using the R software.

3. Results

The methods discussed in the previous section are applied in this section to analyse the survival patterns of elderly patients with at least two diseases within the multimorbidity patterns of GLAD (gastritis, peptic ulcer disease, anxiety, low back pain), CMPD (arthritis, diabetes mellitus, migraine, hypertension) and CPD (asthma, congestive heart failure, stroke).

A total of 154 patients were having diseases that fall under these three categories of disease clusters (Table 1). Of this figure, majority of the patients were having diseases that fall under the CMPD (39.0%), followed by GLAD also having a percentage of 36.3%. Those having diseases that were classified uder CPD constituted 24.7%. Over the entire study period 61 mortalities out of 154 were recorded, of which 52.5%, 32.7% and 14.8% were patients with diseases classified under CMPD, CPD and GLAD respectively. The individuals with diseases in the GLAD cluster appeared to have longer survival, compared to CMPD and CPD (Figure 1).

Table 1: Summary Statistics of Event of Interest

Clusters of Comorbidity	Hospitalized patitients	Discharged	Mortality
GLAD	56 (36.3%)	47 (50.5%)	9 (14.8%)
CMPD	60 (39.0%)	28 (30.1%)	32 (52.5%)
CPD	38 (24.7%)	18 (19.4%)	20 (32.7%)
Total	154	93	61

Table 2: Estimates of the Gompertz Model for GLAD, CMPD, and CPD

	Coefficient	Hazard Ratio (HR)	95% CI for HR	p-value
GLAD	0.000	1.0		
CMPD	1.320	3.76	1.79-7.88	0.0031
CPD	1.350	3.85	1.75-8.46	0.0028
Shape Parameter	0.099			
Rate Parameter	0.003			
Log-likelihood	-256.69			
AIC	521.38			

Figure 2 shows the Gompertz hazard functions for the three multimorbidity patterns. These functions increases exponentially over time, therefore suggesting that Gompertz model is appropriate and consistent with the survival

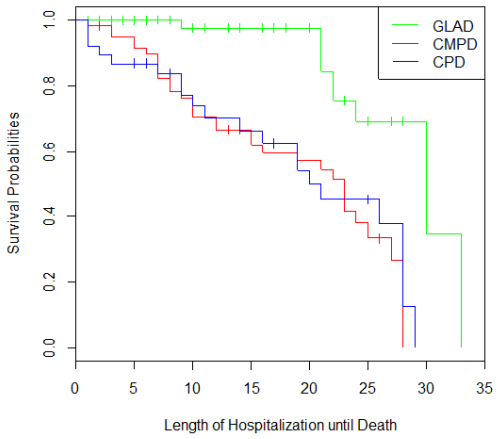

Fig. 1: Kaplan Meier Curves for GLAD, CMPD, and CPD Clusters

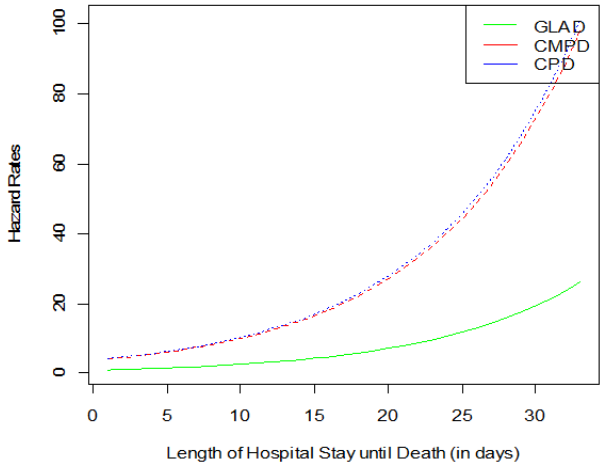

Fig. 2: Gompertz Hazard Functions for GLAD, CMPD, and CPD

data. On the other hand, this implies that the survival data follows the Gompertz distribution. Moreover, from the figure it is evident that the risk for mortality associated with all the multimorbidity partterns increases exponentially over the length of hospital stay. This is consistently and substantially higher for the CPD and CMPD clusters compared to GLAD.

Results from the Gompertz model presented in Table 3 indicates that both CMPD (p-value=0.0031) and CPD (p-value=0.0028) are significantly associated with the survival of patients. The hazard ratio of GLAD is 1.0. The most life threatening cluster is CPD with hazard ratio of 3.85 (95% CI: 1.75-8.46). This suggests that the risk for mortality is 3.85 times increased for those patient with diseases under the CPD cluster. Furthermore, the hazard ratio for mortality corresponding to the CMPD cluster is 3.76 with (95% CI: 1.79-7.88). This imply that the individuals with diseases in the CMPD cluster have 3.76 increase risk for mortality, compared to those patients with diseases in the GLAD cluster. From the Hazard Ratios it is evident that both CPD and CMPD clusters have similar effect on the survival time of patients.

The shape and scale parameters of the Gompertz model are 0.099 and 0.003 respectively. The shape parameter is greater than zero (0) therefore suggesting that the risk for mortality associated with the three comorbidity clusters increases exponentially over the length of hospital stay. This reinforces the results in Figure 2, therefore giving a confirmation that the survival pattern of the patients in the observed data is Gompertz distributed. Hence the fitted Gompertz model is appropriate.

4. Conclusion

This paper has studied the extent at which different comorbidity clusters, thus GLAD, CMPD and CPD influences the survival of elderly patients. We found that the hazards for mortality of the elderly patients with these multiple disorders increases exponential with the length hospital stay. The extent of increment is largely influenced by the kind of diseases that constitute a cluster. Specifically, the multimorbidity partterns of CPD (asthma, congestive heart failure, stroke) and CMPD (arthritis, diabetes mellitus, migraine, hypertension) are seriously life threatening, compared to GLAD (gastritis, peptic ulcer disease, anxiety, low back pain). The findings of this study draw attention to the importance of avoiding the mechanisms underlying the susceptibility of multimorbidity patterns or cluster comorbidities, particularly those clustering cardiovascular, metabolic and pulmonary diseases in order to reduce their health burden.

References

[1] M Fortin, L Lapointe, C Hudon, A Vannasse, AL Ntetu, and D Maltais. Multimorbidity and quality of life in primary care: a systematic review. *Health and Quality of Life Outcomes*, 2:51, 2004.

[2] C Hudon, H Soubhi, and M Fortin. Relationship between multimorbidity and physical activity: Secondary analysis from the quebec health survey. *BMC Public Health*, 8:304, 2008.

[3] M Hunger, B Thorand, M Schunk, A Döring, P Menn, A Peters, and R Holle. Multimorbidity and health-related quality of life in the older population: results from the german kora-age study. *Health and Quality of Life Outcomes*, 9:53, 2011.

[4] MM Islam, JM Valderas, L Yen, P Dawda, T Jowsey, and IS McRae. Multimorbidity and comorbidity of chronic diseases among the senior australians: Prevalence and patterns. *PLoS ONE*, 9(1): e83783. doi:10.1371/journal.pone.0083783, 2014.

[5] UT Kadam, PR Croft, and North Staffordshire GP Consortium Group. Clinical multimorbidity and physical function in older adults: a record and health linkage study in general practice. *Family practice*, 24:412–419., 2007.

[6] I Kirchberger, C Meissenger, M Heier, A-K Zimmermann, B Thorand, CS Autenrieth, A Peters, K-H Ladwig, and A Döring. Patterns of multimorbidity in the aged population. results from the KORA-Age study. *PloS ONE*, 7(1):e30556. Doi: 10.1337/journal.pone.0030556., 2012.

[7] DG Kleinbaum and M Klein. *Survival analysis. A self learning text.* New York, Springer, 2005.

[8] B Moghimi-Dehkordi, A Safaee, MA Pourhoseingholi, R Fatemi, Z Tabeie, and MR Zali. Statistical comparison of survival models for analysis of cancer data. *Asian Pacific Journal of Cancer Prevention*, 9:417–420, 2008.

[9] FT Oduro and R Tawiah. Impact of multi-morbidity patterns on length of hospitalization and mortality: A study of elderly general clinic patients at a hospital in ghana. *Journal of the Ghana Science Association*, 14:35–44, 2012.

[10] A Prados-Torres, B Poblador-Plou, A Calderón-Larra naga, LA Gimeno-Feliu, F González-Rubio, A Poncel-Falcó, A Sicras-Mainar, and JT Alcalá-Nalvaniz. Multimorbidity patterns in primary care: Interraction among chronic diseases using factor analysis. *PLos ONE*, 7(2): e32190. doi: 10:1371/journal.pone 0032190., 2012.

[11] R Ravangard, M Arab, A Rashidian, A Akbarisari, A Zare, and H Zeraati. Comparison of the results of cox proportional hazards model and parametric models in the study of length of stay in a tertiary teaching hospital in tehran, iran. *Acta Medica Iranica*, 49:650–658, 2011.

[12] I Schäfer, E-C von Leithner, G Schön, D Koller, H Hansen, T Kolonko, H Kaduszkiewwicz, K Wegscheide, G Glaeske, and H van den Busche. Multimorbidity patterns in the elderly: A new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS ONE*, 5(12): e15941 doi: 10:1371/journal.pone: 0015941, 2010.