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FACULTY OF SCIENCES
Master of Statistics

Master's thesis

Implementation of the Care Pathway for Primary Palliative Care in 5 regions in Belgium (pro-Spinoza)

Supervisor :
Prof. dr. Tomasz BURZYKOWSKI

Supervisor :
Dr. BERT LEYSEN

Felix Tabotson Abang

Thesis presented in fulfillment of the requirements for the degree of Master of Statistics

Transnational University Limburg is a unique collaboration of two universities in two countries: the University of Hasselt and Maastricht University.

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Abstract

The aging nature of our societies and the insufficient attention to the complex needs of older people, make Palliative Care an in important Public health issue. This calls for a need not only to improve health by preventing disease and disability but also to improve the quality of life that remains, enabling people to live well and, when the time comes, to die well. The goal of Palliative care is to improve the symptoms, dignity and quality of life of people approaching the end of their lives and on the care of and support for their families and friends.

This primary palliative care is an emerging field in Belgium. The Care Pathway for Primary Palliative Care (CPPC), developed at the University of Antwerp, is aimed at helping primary health care workers to provide high quality palliative care. Starting from early identification of palliative patients which was through asking a surprise question by the general practitioners (GPs), patient- and family-centered care is believed to be delivered towards the end of life.

The objective of this thesis was to investigate whether there are patterns of health care delivery over time in the last year of life, to be recognized overall, per cluster, per disease category, and or per social status.

Due to the clustered nature of the data or repeated measurements of the response variables for this thesis; the existence of over-dispersion as a result of the variance being larger than the mean and the occurrence of excess zeros beyond what a Poisson model can incorporate, the extensions of the Poisson model were considered. These include Zero-Inflated Negative Binomial model to account for the Overdispersion in the data, the so-called Zero-Inflated Poisson-Normal-Gamma model to account for excess zeros in the data, Zero-Inflated Mixed-Effects Poisson Model to account for patient-specific effects and a marginalized multilevel model to provide the population-average interpretation of the parameters.

As regards to cancer, dementia and social status, the probability of 0 day of stay per week in the Palliative Care Unit depends only on cancer. At cluster level, this probability depends

on cancer and social status of the patients and marginally, it depends solely on cancer. The expected number of days in the Palliative Care Unit was found to be related to cancer, dementia and social status only at cluster level. Thus, there were patterns of health care delivery over time in the last year of life as recognised overall, per cluster, per disease category, and or per social status of the patients.

1 INTRODUCTION

The aging nature of our societies and insufficient attention to the complex needs of older people make Palliative Care an in important Public health issue. This provides a need not only to improve health by preventing disease and disability but also to improve the quality of life that remains, enabling people to live well and, when the time comes, to die well (EAPC, 2010). The goal of Palliative care is to improve the symptoms, dignity and quality of life of people approaching the end of their lives and on the care of and support for their families and friends(EAPC, 2010).

Therefore Palliative care is seen as a health issue that provides relief from pain, affirms life and regards death as a normal process. It intends neither to hasten or postpone death and integrates the psychological and spiritual aspects of patient care. Furthermore, it is applicable early in the course of illness, together with other therapies that are intended to prolong life and includes those investigations needed to better understand and manage distressing clinical complications(WHO, 2010).

Palliative has often been neglected and is mostly offered to people with cancer in hospice settings. It is now offered more widely and integrated more broadly across health care services. populations worldwide are aging, leading to a dramatic increase in the numbers of people living into their seventies, eighties and nineties. Further more, patterns of disease in the last years of life are also changing, with more people dying from chronic debilitating conditions, like cardiovascular disease, chronic obstructive pulmonary disease, diabetes, cancer and dementia(Ferri CP et al., 2005). It is known that many of these illnesses often occur among older people, who mostly experience multiple health problems and disabilities.

Symptoms such as pain, anorexia, low mood, mental confusion, constipation, insomnia and problems with bladder and bowel control often occur in their last year of life(Addington-Hall J

et al., 1998).

Palliative care services need to be developed to meet the complex needs of older people and these services need to be available for people with diseases other than cancer and offered based on need rather than diagnosis or prognosis. These palliative services could be integrated in primary care(Pro-Spinoza, 2011).

This primary palliative care is an emerging field in Belgium. The Care Pathway for Primary Palliative Care (CPPC), developed at the University of Antwerp, aimed at helping primary health care workers to provide high quality palliative care. Starting from early identification of palliative patients which was through asking a surprise question by the general practitioners (GPs), patient- and family-centered care is believed to be delivered towards the end of life(Pro-Spinoza, 2011).

To this effect, a stepped wedge cluster design was set up with 5 regions being 5 clusters. Volunteered General Practitioners(GPs) were involved in recruiting people with reduced life expectancy and their informal care giver. The quality of care was measured, first, by the web-based questionnaires filled by GPs and patients in a secured platform, and second, by health care consumption data in the last year of life. Within and between the stepped wedge clusters, a prospective cohort as well as a case control design were developed. For this case control design, health care consumption data have been collected for all people domiciled in the research clusters having died a 'non-sudden' death during the study period(Pro-Spinoza,2011).

The primary outcome of this quantitative part was hospital admission rate in the last year of life and secondary outcomes were death at home, health care consumption, and quality of care as perceived by the web-questionnaires. To evaluate the implementation in a qualitative way, a multiple case study design was used and focus groups were meant to reveal the strategies every region used in improving the local palliative care organization. At the end, a semi-structured interviews were put in place to find how the general practitioners implement the Care Pathway for Primary Palliative Care and how patients and/or informal carers experience receiving the

Care Pathway for Primary Palliative Care(Pro-Spinoza, 2011).

For this Master thesis, the focus was the analysis of the health care consumption data of 4 of the 5 clusters, of which data were available. No data were available on patients to whom the intervention was given. The objective was to investigate whether there are patterns of health care delivery over time in the last year of life, to be recognized overall, per cluster, per disease category, or per social class.

Due to the clustered nature of these data or repeated measurements of the response; the existence of over-dispersion as a result of the variance being larger than the mean and the occurrence of excess zeros beyond what a Poisson model can incorporate, the extensions of the Poisson model was considered (Kassahun et al.,2014). These involve Zero-Inflated Negative Binomial model to account for the Overdispersion in the data, the so-called Zero-Inflated Poisson-Normal-Gamma model to account for excess zeros in the data, Zero-Inflated Mixed-Effects Poisson Model to account for patient-specific effects and a marginalized multilevel model to provide the population-average interpretation of the parameters.

2 MATERIAL AND METHODS

2.1 Data Description

This study was a multivariate longitudinal observational in which a number of different responses were measured repeatedly over time on a particular patient. The data in this study, comprises of two data sets: the consumption data set which consisted of the response variables and the patient data set which consisted of the explanatory variables. In total, there were 102,762 observations, obtained from 17,112 patients (aged 45 years and older).

The length of stay or the number of days in different settings (hospital, nursing homes and palliative care units) and the number of home visits by a patient own GP, characterized by excess zero counts, were taken from each patient who was in his or her last year of life. The age category of patient and GP, gender of patient, place of death of patient, month of death, family size, dependency of help, financial measures, palliative forfeit requested, attestation of chronic disease, cancer, dementia, patient's GP and territories of palliative care networks and GPs circles, were also recorded from each patient. Table 1 gives a brief description of the variables contained in the data .

The response variables; the number of days in different settings and the number of home visits by a patient own GP, were measured repeatedly per time points which are stratified into time frames and are characterized by excess zero counts. The explanatory variables on their part, consisted mostly of categorical variables.

Table 1: A Description of the Variables

Response Variable	
Variable	Description
NO_HOSPDAYS	Number of hospitalisation days per time frame without stay in palliative care unit
NO_PALLU	Number of days in the palliative care unit per time frame
WZC	Number of days in the nursing home
WZC_KORT	Number of days in the short stay department of a nursing home
TV_DAYS	Total number of days with home care nursing
TV_P_DAYS	Number of home care nursing days with an official palliative care approach
HA_HB	Number of home visits by own GP
Explanatory Variable	
Variable	Description
ID	National number of patient at least 45 years old
GP_CHOICE	The Patient's GP
GP_AGE05_CAT	Age Category of GP: Per 5 Years
KANKER	0= No Cancer, 1 = Cancer
DEMENT	0 = No Dementia, 1 = Dementia
CLUSTER	Territories of palliative care networks(1=Antwerp ; 2= Mons; 4=Brussels; 5=Limburg)
SUBCLUSTER	Territories of GP Circles
GENDER	0=Female, 1= Male
AGE05_CAT	Age Category Patient, Per 5 Years
MAJOR_COVERAGE_YN	0=Normal reimbursement; 1= Higher reimbursement (low social-economic status)
CHRONZ_ATTEST	0=No Attestation for a chronic disease;1= Attestation for a chronic disease
FAM_SIZE	Family Size (1 : 1 Person, 2 : 2 Persons,....., 12: 12 or more Persons)
PF	0=No Palliative Forfeit requested; 1= Palliative Forfeit requested
DEPENDANCY	Dependancy of help
MAF	MAF is a Financial Measure of how much a family spend for health care(0=MAF limit not exceeded;1=MAF limit exceeded).
CHRONZ_FF	0=No Forfeit for chronic disease;1=Received Forfait for chronic disease
GMD	A 'GMD' is a Financial Measure to bind patients to their general practitioners (0=no GMD; 1=has GMD)
PLOD	Place of Death (1=at home; 2=nursing home; 3=hospital; 4=palliative care unit; 5=anywhere else).
PERIOD_D	Month of Death
TIMEFRAME	1=[12M,6M[, 2=[6M,3M[, 3=[3M,1M[, 4,=[1M,2W[, 5=[2W,1W[, 6=[1W,date of death[

2.2 Exploratory Data Analysis(EDA)

Prior to statistical modeling, the EDA was performed using graphs to gain a substantial insight into the data. To achieve this, the individual profile of each outcome was plotted which gives a comparison of the between- and within-patient variability. A mean profile of each outcome was also plotted to visualize how the proportion of the length of stay in different settings and of home visits by a patient own GP vary over the time frame. Further, a variance structure was not left out to provide a picture of the type of model to be fitted.

2.3 Statistical Analysis

Count data are most commonly modeled using the Poisson model. Due to issues like clustering in the data, repeated measurements of the response; the existence of overdispersion and the occurrence of excess zeros beyond what a Poisson model can incorporate, the extensions of the Poisson model is usually considered (Kassahun et al.,2014). Such issues can effectively be accounted for through the use of random subject-specific effects (Molenberghs and Verbeke, 2005), through the use of an Overdispersion model, such as, the negative-binomial model for count data (Breslow, 1984; Lawless, 1987) and through the use of the so-called zero-inflated models(Lambert ,1992; Greene, 1994), respectively.

To this effect, in order to investigate whether there are patterns of health care delivery over time, to be recognized overall, per cluster, per disease category or per social status or class, Poisson models, Negative Binomial models, Zero-Inflated Models; Zero-Inflated Negative Binomial models ; a Mixed-Effect Poisson Models and a Marginalized Zero-Inflated Combined Models were used . Since the Data

set for this study is characterized by excess of zero counts, these excess zero counts must be accounted for. Accounting for the excessive zeros assumes that zeros may come from two processes: a point-mass or a Poisson-normal-gamma process, as a mixture, leading to Zero-Inflated Poisson-Normal-Gamma model- ZI(PNG) (Kassahun et al., 2014), as a good start to analyse this data set.

2.3.1 Standard Poisson Models

Poisson regression model is traditionally known to model count data. Unlike the familiar Gaussian distribution which has two parameters N(μ,σ^2), the Poisson distribution is described by a single parameter, λ as both the mean and the variance. Thus a Poisson distribution is characterized by two parameters having the same value, the expected value (mean) and the variance. This can be a strong assumption. However, this does not always apply to count data. It is not usually uncommon that the observed variance of a count variable is greater than the observed mean, a situation referred to as over-dispersion. In this case, using Poisson regression to model data is not appropriate.

When there is over-dispersion, as a consequence of omission of important covariates, data in question can be modeled using Negative Binomial (NB) regression model. Negative binomial regression, like Poisson model, examines the relationship between predictors and count dependent variable through log link, which assumes a mixture distribution for count variable.
Suppose that $Y_i \sim Poisson(\lambda_i)$, where λ_i is a random variable with gamma distribution, with mean $E(\lambda_i) = \mu_i$ and variance, $var(\lambda_i) = \frac{\mu_i}{k}$. Then the unconditional distribution of Y_i is Negative Binomial with the probability density function given by:

$$f(Y_i = y_i) = \frac{\Gamma(y_i + k)}{\Gamma(k) y_i!} \left(\frac{k}{k + \mu_i}\right)^k \left(\frac{\mu_i}{k + \mu_i}\right) y_i$$

This distribution has mean, $E(Y_i) = \mu_i$ and variance, $Var(Y_i) = \mu_i(1+\mu_i k^{-1})$, where k is the dispersion parameter. When $k = 1$, the mean and the variance become same, and thus Negative Binomial distribution will be reduced to Poisson distribution. On the other hand, when $k^{-1} > 0$, the variance will exceed the mean and the distribution will be overdispersed. A characteristic feature of this distribution is that it accounts only for overdispersion, not for underdispersion (i.e. the variance is smaller than the mean).

2.3.2 Zero-Inflated Models

When the data are characterized by excess zero counts, the data can no longer be modeled using Ordinary Poisson Regression Model. There exists substantial literature on the modeling of these zero-inflated count data using the Hurdel Model(Mullahy, 1986) and the Zero-Inflated Poisson model (Lambert, 1992).

The hurdle model is seen as a two-part model for count data. The first part is the model for the binary variable which indicates whether the response outcome is zero or positive. Conditional on a positive outcome, the second part of the model uses a truncated Poisson distribution or a truncated Negative Binomial (NB) distribution to model the positive variable. Let Y_i denote the observation matrix for subject i (i = 1, ..., n). The probability $P(Y_i > 0) = 1 - P_i$ and $P(Y_i = 0) = P_i$. A logistic

regression model was used for P_i and a log-linear model was used for the mean of the truncated Poisson distribution or truncated Negative Binomial (NB) distribution. However, when the non-zero part is a discrete random variable, a popular approach to analyse count data with excess zeros is to use a zero-inflated Poisson (ZIP) regression model (Lambert, 1992).

In zero-inflated poisson models, it is assumed that there are two processes that can generate zeros. The first process generates only zeros (ie the zeros can come from a point mass) with probability, say π_{ij} for observation i at time point j, and the second process generates counts (ie from count components) with probability, say 1 - π_{ij} (Hinde and Demetrio, 1998). The general form of the zero-inflated poisson-normal -gamma model is given as follows:

$$Y_{ij} \sim \begin{cases} 0 & \text{with probability} \pi_{ij}, \\ f_i(y_{ij}|b_{1i}, \xi, \theta_{ij}) & \text{with probability} (1-\pi_{ij}), \end{cases}$$

,

which leads to the probabilities $P(Y_{ij} = y_{ij}|b_{1i}, \xi, \theta_{ij}, \pi_{ij})$ given by

$$P(Y_{ij} = y_{ij}|b_{1i}, \xi, \theta_{ij}, \pi_{ij}) \sim \begin{cases} \pi_{ij} + (1-\pi_{ij}) f_i(0|b_{1i}, \xi, \theta_{ij}) & if y_{ij} = 0, \\ (1-\pi_{ij}) f_i(y_{ij}|b_{1i}, \xi, \theta_{ij}) & if y_{ij} > 0, \end{cases}$$

where Y_{ij} is the jth outcome measured for subject i = 1,.....,N, j = 1,.....ni; $b_i \sim$ N(0,D), and $\theta_{ij} \sim$ Gamma(α,β), x_{ij} and z_{ij} are p-dimensional and q-dimensional vectors of known covariates, and ξ is a p-dimensional vector of unknown fixed regression coefficients.
The zero-inflated component $\pi_{ij} = \pi(x'_{ij}\xi + z'_{ij}b_{2i})$ can be modeled using a Bernoulli model having only an intercept in its simplest form, with x_{2ij} and z_{2ij} as covariates and β as a vector of zero-inflated coefficients to be determined together with the random effects b_{2i} (Kassahun et al., 2014). In modeling, the link function such as logit or probit could be applied. On the other hand, the covariates x_{1ij} and z_{1ij} together with b_{2i} are used on the non-zero count part.
It should be noted that in fitting this model, the covariates in the count and zero-inflation component can either be overlapping, a subset of the regressors can be used for the zero-inflation, or entirely different covariates for the two parts can be used (Kassahun et al., 2014).

Also, the Variance-Covariance matrix, where the random effects are assumed to be normally distributed and possibly correlated with correlation parameter ρ, is given by

$$D = \begin{pmatrix} d_1 & \rho\sqrt{d_1}\sqrt{d_2} \\ \rho\sqrt{d_1}\sqrt{d_2} & d_2 \end{pmatrix},$$

where d_1 is the Standard deviation of the non-zero part random effect, d_2 is the Standard deviation zero part random effect and ρ is the Correlation of random effects.

Furthermore, the conditional mean and variance of this Zero-Inflated Poisson-Normal-Gamma model, ZI(PNG), are stated as:

$$E(Y_{ij}|b_{1i}, \xi, \theta_{ij}) = \theta_{ij} k_{ij} (1\pi_{ij})$$

,

$$Var(Y_{ij}|b_{1i}, \xi, \theta_{ij}) = \theta_{ij} k_{ij} (1 - \pi_{ij})[1 + \theta_{ij} k_{ij} (\pi_{ij} + 1/\alpha)]$$

.

From the variance expression, it can be seen clearly that the conditional variance is inflated as a result of either overdispersion in the data (parameter α), or as a result of zero-inflation (parameter π_{ij}), or both.

2.3.3 Estimation

The Likelihood estimation of the Poisson- Normal-Gamma is obtained by integrating over the random effects, combining the marginal likelihood, and maximizing it in the usual way. This can also be marginalized analytically over the gamma random effect, with further numerical integration over the normal random effects Molenberghs et al. (2007) and Molenberghs et al. (2010). This enables the use of a flexible normal random-effects tool such as the SAS procedure NLMIXED (Kassahun et al., 2014). The partially marginalized Poisson- Normal-Gamma takes the form:

$$f(y_{ij}|b_{1i}, \xi) = \int f(y_{ij}|b_{1i}, \xi, \theta_{ij}) f(\theta_{ij}, \alpha_j, \beta_j) \mathrm{d}\theta_{ij}$$

$$= \binom{\alpha_j + y_{ij} - 1}{\alpha_j - 1} \cdot \left(\frac{\beta_j}{1 + k_{ij}\beta_j} \right)^{y_{ij}} \cdot \left(\frac{1}{1 + k_{ij}\beta_j} \right)^{\alpha_j} . {k_{ij}}^{y_{ij}}$$

Applying this to the Zero-Inflated Poisson-Normal-Gamma, we get that:

$$f(y_{ij}|b_{1i}, \xi, b_{2i}, \beta) = I(y_{ij} = 0)\pi_i j + \binom{\alpha_j + y_{ij} - 1}{\alpha_j - 1} \cdot \left(\frac{\beta_j}{1 + k_{ij}\beta_j} \right)^{y_{ij}} \cdot \left(\frac{1}{1 + k_{ij}\beta_j} \right)^{\alpha_j} . {k_{ij}}^{y_{ij}},$$

with $\pi_{ij} = \pi(x'_{2ij}\gamma + z'_{2ij}b_{2i})$.

2.4 Zero-Inflated Negative Binomial Models

In order to account for overdispersion in these data, a Zero-Inflated Negative Binomial Model was considered. The Zero-Inflated Negative Binomial (ZINB) regression model assumes that there are two distinct data generation processes. For observation i, with probability π_i the only possible response of the first process is zero counts, and for the second process, the response with probability of $(1 - \pi_i)$ is governed by a negative binomial with mean λ_i. The zero counts are generated from both the first and second processes, where a probability is estimated for whether zero counts are from the first or the second process. The overall probability of zero counts is the combined probability of zeros from the two processes.

According to Greene(1994) and Yau et al.(2003) , a ZINB model for the response Y_i can be formulated as:

$$\begin{cases} Y_i = 0 & \text{with probability } \pi_i, \\ Y_i \sim \text{negative binomial}(\lambda_i, k) & \text{with probability } (1-\pi_i), \end{cases}$$

so that

$$P(Y_i = 0) = \pi_i + (1-\pi_i)(1+\lambda k_i)^{\frac{-1}{k}}$$

$$P(Y_i = y_i) = (1-\pi_i)\frac{\Gamma(y_i + 1/k)}{\Gamma(y_i+1)} . \frac{(k\lambda_i)^{y_i}}{(1+k\lambda)^{(y_i+1/k)}}, y_i = 1, 2, ...$$

As such, the mean and variance of the Y_i are

$$E(Y_i) = (1-\pi_i)\lambda_i$$

and

$$V(Y_i) = (1-\pi_i)\lambda_i(1+\lambda(\pi_i + k))$$

,
where λ_i is the mean of the underlying negative binomial distribution, and k is the overdispersion parameter. It should be noted that when k tend to zero, the zero-inflated negative binomial reduces to zero-inflated poisson. The parameter π_i, often known as the zero-inflation factor, is the probability of zero counts from the binary process and can be modeled as: $logit(\pi_i) = Z_i\xi$, where ξ is the $(q+1) \times 1$ vector of zero-inflated coefficients to be estimated and is associated with the known zero-inflation covariate vector $Z_i = (1, Z_{i1}, , Z_{iq})$, where q is the number of the covariates Zs not including the intercept. The parameter λ_i is modeled as a function of a linear predictor as: $\lambda_i = exp(X_i\beta)$, where β is the $(p+1) \times 1$ vector of unknown parameters associated with the known covariate vector $X_i = (1, X_{i1}, , X_{ip})$, where p is the number of covariates not including the intercept.

2.5 Zero-inflated Mixed-Effects Models

Models such as the Negative Binomial, Zero-Inflated Poisson and Zero-inflated Negative Binomial mentioned above, were based on assumption of independence of the responses. In this study, the observations were repeatedly measured per subject or were clustered of observations within a subject and so the above assumptions could no longer hold. A Mixed-Effects Models are a natural choice since there is obviously correlation within the repeated measurement of the same patient. Therefore, the validity of statistical inference in such a case can be hindered by the previous models(ie NB, ZINB and ZIP).

The introduction of the random effects into regression models can efficiently account for correlation in the response and variability within subjects. As well noted, Hall (2004) extended the Lambert(1992) zero-inflated count models to accommodate longitudinal data, by adding a random effect to account for the within-subject correlation in the count data. Min and Agresti (2005) proposed a general case by adding random effects in both components. Let Y_{ij} be the observation j (j = 1,.....,t_i) for subject

i (i= 1,.....,n and let the b_i=$(b_{1i}, b_{2i})'$ be the random effects meant to account for within-subjects correlations. The models for λ_{ij} and π_{ij} are stated as:

$$log(\lambda_{ij}) = x_{ij}\beta + z_{1ij}b_{1i}$$

,

$$logit(\pi_{ij}) = x_{ij}\gamma + z_{2ij}b_{2i}$$

where x_{ij} and z_{1ij} are the covariate vectors pertaining to the fixed and the random effects respectively. Furthermore, we assume that b_{1i} and b_{2i} are normally distributed and possibly correlated or even uncorrelated.

2.6 Marginalized Zero-Inflated Combined Model

The generalized linear mixed model of Molenberghs and Verbeke(2005) and its extention for overdispersion of Molenberghs et al.(2010), together with data hierarchy and zero-inflation (Min and Agresti, 2005), do not provide population averaged interpretation for regression parameters, of which such results are usually needed in practice(Kassahun et al., 2014).

A marginalized multilevel model (MMM) is proposed by Heagerty (1999) and Heagerty and Zeger (2000), by simultaneously defining a marginal mean and a conditional mean by considering the so-called connector function, yields marginally interpretable covariate effects (Kassahun et al., 2014).

In this section, overdispersion and correlation of these count data with excess zeros wil be accounted for by using the combined model idea of Molenberghs et al.(2010) and the marginalized multilevel model of Heagerty (1999), together with concepts of zero-inflated models, and a marginalized zero-inflated combined model as a alternative modeling strategy (Kassahun et al., 2014) . It should be noted that the Population averaged interpretation is possible not only for the positive count component, but also for the zero-inflation component (Kassahun et al.,2014).

The conditional zero-inflated combined model which assumes mixing of zeros with probability π_{ij}^c and counts from a poisson-gamma normal process with probability 1 - π_{ij}^c,can be formulated as:

$$P(Y_{ij} = y_{ij}|b_i, \xi, \theta_{ij}, \phi, \pi_{ij}^c) = \begin{cases} \pi_{ij}^c + (1-\pi_{ij}^c)f_i(0|\lambda_{ij}^c, \theta_{ij}) & if y_{ij} = 0, \\ (1-\pi_{ij})f_i(y_{ij}|\lambda_{ij}^c, \theta_{ij}) & if y_{ij} > 0, \end{cases}$$

where $\pi_{ij}^c = \Phi(\Delta_{ij1} + z'_{ij1}b_{i1})$, $\lambda_{ij}^c = \theta_i jexp(\Delta_{ij2} + z'_{ij1}b_{i2})$, $b_i = (b_{i1}, b_{i2})' \sim N(0, D)$; and $\theta_{ij} \sim Gamma(\alpha, \beta)$. In addition, Δ_{ij1} and Δ_{ij2} are connector functions of the zero part and the positive count part, corresponding to the random vectors b_{i1} and b_{i2} and regressors z_{ij1} and z_{ij2}, respectively. And the marginal formulation is as follows:

$$P(Y_{ij} = y_{ij}) = \begin{cases} \pi_{ij}^m + (1-\pi_{ij}^m)f_i(0|\lambda_{ij}^m) & if y_{ij} = 0, \\ (1-\pi_{ij}^m)f_i(y_{ij}|\lambda_{ij}^m) & if y_{ij} > 0, \end{cases}$$

where $logit(\lambda_{ij}^m) = x'_{ij1}\gamma^m$ and $ln(\lambda_{ij}^m) = x'_{ij2}\xi^m$, with known covariates x'_{ij1} and x'_{ij2} and a vector of zero-inflation coefficients γ and ξ.
It should be noted that in modeling, $ZI(PNG)_l$ or $ZI(PNG)_p$ denotes the conditional zero-inflated combined model,depending on the first-process link function applied(Kassahun et la., 2014).

2.6.1 Estimation

Let us first consider the models with zero-inflation but without marginalization. The probability resulting from $ZI(PNG)$ or $ZI(PNG)_p$, marginal over θ_{ij} but still conditional upon the normal random effect b_i, is given by:

$$f(y_{ij}|b_i, \xi, \theta_{ij}, \phi, \pi_{ij}) = I(y_{ij} = 0)\pi_i^c j + (1 - \pi_{ij}^c)g_1(b_i)$$

, and the likelihood for ZI(PNG) is stated as:

$$L(\xi, \gamma, D, \phi) = \prod_{i=1}^{N} \int \prod_{j=1}^{n_i} \{\pi_{ij}^c(b_i) + (1 - \pi_{ij})^c(b_i)g_2(b_i)\}^{I(y_{ij}=0)} \times \{(1 - \pi_{ij}^c)(b_i)g_1(b_i)\}^{1-I(y_{ij})}\phi(b_i, D)\mathrm{d}b_i,$$

where

$$g_1(b_i) = \left(\alpha_j + y_{ij} - 1\alpha_j - 1\right) . \left(\frac{\beta_j}{1 + k_{ij}\beta_j}\right)^{y_{ij}} . \left(\frac{1}{1 + k_{ij}\beta_j}\right)^{\alpha_j} . {k_{ij}}^{y_{ij}}$$

,

$$g_2(b_i) = \left(\frac{1}{1+k_{ij}\beta_j}\right)^{\alpha_j}$$

2.7 INFORMATION CRITERIA

In order to select our model, the Akaike information criterion (AIC) (Akaike, 1973) was used and is calculated as follows: $AIC = -2 \times ln(L) + 2p$, where L is the ML or REML of the fitted model and p is the total number of parameters being estimated in the model. AIC provides a way to compare any two models fitted to the same set of observations; i.e., the models do not need to be nested. A smaller value of AIC indicates a better fit of the model. The Bayesian information criterion (BIC) was also used (values not shown) to assess the fit of a model and is calculated as:$BIC = -2 \times ln(L) + p \times ln(n)$, where n is the total number of observations used in estimating the model. Model with smaller value of BIC was considered a better fit of the model.

2.8 SOFTWARE

In this study, SAS version 9.3 was used to performed all the necessary statistical analysis of model fitting and all p-values ¡ 0.05 were considered statistically significant. Proc GENMOD and Proc GLIMMIXED were used to obtain the starting values and also in fitting the model with assumed Poisson distribution and Negative Binomial distribution. Proc NLMIXED was used to fit ZINB model, Zero-Inflated mixed-Effects model,ZI(PNG) and Marginalized Zero-Inflated Combined model(MZI).

3 RESULTS

This section made known the exploratory data analysis' findings and the results of the various statistical analysis on fitted models for the outcomes variables: the number of days in the different settings (hospital, nursing homes, home care nursing, palliative care units) and the number of home visits by a patient own GP.

3.1 Exploratory Data Analysis

3.1.1 Summary Statistics

The data used in this study as earlier mentioned, consisted of 102,762 observations from 17,112 patients of aged 45 years and older. These data comprise of two data set: the Consumption data containing the response variables and the Patient data which contain the explanatory variables. Table 2 shows the summary statistics of the response variables.

Table 2: Summary Statistics For Response Variables

Variable	N	Mean	Std Dev	Variance	Minimum	Maximum
NO_HOSPDAYS	102672	6.0282	24.6424	607.2495	0	2190
TV_P_DAYS	102672	1.5076	10.4491	109.1840	0	181
WZC_KORT	102672	0.1940	2.8539	8.1448	0	181
NO_PALLU	102672	0.2170	2.0082	4.0330	0	111
TV_DAYS	102672	12.3620	33.3000	1108.8900	0	181
HA_HB	102672	1.9458	3.4528	11.9220	0	93
WZC	102672	16.5533	40.14298	1611.4600	0	356

It can be observed that the variance of each response is quite larger than the corresponding mean and this huge difference is seen clearly for the response variable: the number of days in nursing homes, having mean value of 16.5533 and variance of 1611.4600. This is closely followed by the response variable: the total number of days with home care nursing which has a mean of 12.3620 and variance of 1108.8900. This indicates the presence of overdispersion in the data which has to be accounted for in the analysis.
It can also be seen that the response variable: the number of hospitalisation days, has the minimum value 0 and maximum value 2190, which is the highest among the responses and this closely followed by the response variable, the number of days in the nursing home, with minimum value 0 and maximum value 356. This indicates that most patients stay more in the hospitals than in the other settings.
On the other hand, Table **5** of **APPENDIX A** presents the summary statistics for the explanatory variables. It can be observed that most of the variables have minimum value 0 and maximum value 1. Unlike in Table 2, the variances are less than the mean of the variables except for time variable.
The histograms in Figure **7,8,9,10** of **APPENDIX A** pick at 0 indicating that most patients have 0 day of stay in all the settings. It can be seen that 10,241 patients (59.85%) had 0 day of stay in the hospital, 16364 patients (93.68%) had 0 day of home care nursing days with an official palliative care approach, 16,948 patients (99.04%) had o day in the department of a nursing home, 16687 patients

(97.52%) had 0 day of stay in the palliative care unit, 11,983 patients (70.02%) had 0 day of stay with home care nursing, 8,652 patients (50.56%) had 0 day of home visits by own GP and 11,672 patients (68.21%) had 0 day of stay in the nursing home.

It can also be observed from Figure **7,8,9,10** of **APPENDIX A** that the outcomes variables do not follow normal distribution. The histograms clearly showed that the observations are non-negative and are skewed to the right. This further contributes to the reason why the so-called Zero-Inflated Poisson models were chosen to perform the statistical analysis for these data.

3.1.2 Individual Profiles

The distribution of the outcome variables was seen to be non-negative and skewed to the right from the histograms in Figure **7,8,9,10** of APPENDIX A. Also, of 102,672 observations , only about 20,534 of the observed number of days stay in different settings and of home visits by a patient own GP were non-zero (ie almost 80% are zero), indicating that there is a non-negligible dominance of zero counts in the data. These render the outcome variables to be adequate for the fit of the so-called Zero-Inflated Poisson Models. Actually, the proportion of the number of days stay in various settings and of home visits by a patient own GP per time frame was considered so as to take into account the length of stay in different settings per time frame. As clearly noticed, measurements were taken repeatedly over time and as such each of the outcome variable within patients is expected to be correlated and those measurements within patients are expected to be more similar than between patients. This can be seen in Figure 1, 2, 3 which show the profiles of number of days of various settings for 250 randomly selected subjects where the profiles touch the zero-axis many times except for some settings.
Further, much between- and within-patient variability were observed for the number of days in hospital, the number of days in nursing homes, the number of days in home care nursing, the number of days in home care nursing with palliative care approach and as well as the number of days of home visits by own GP. Precisely, at time frame 1, there is high variability in the intercepts for all stay settings and the patients seem to evolve in a similar way. These variability are very much less observed in the number of days in palliative care units and number of days in the short stay department of a nursing home.

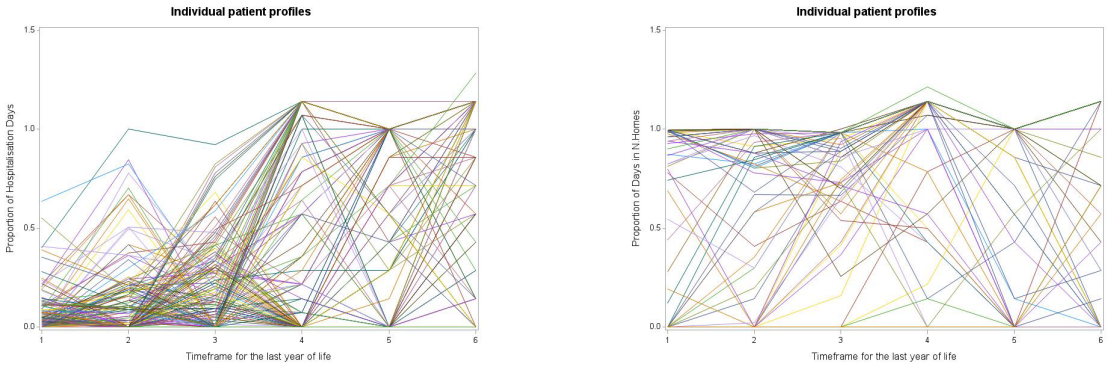

Figure 1: Individual Profiles For Hospdays and Days in N.Homes

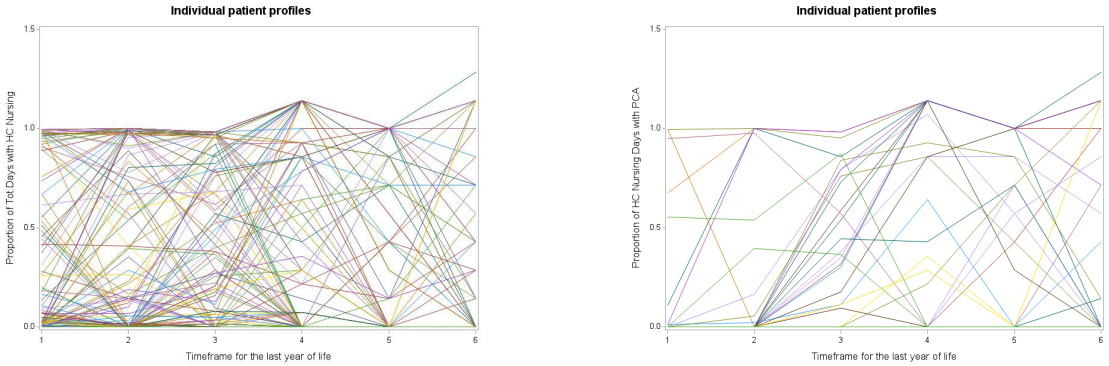

Figure 2: Individual Profiles For Days with HC Nursing ang HC Nursing with PCA

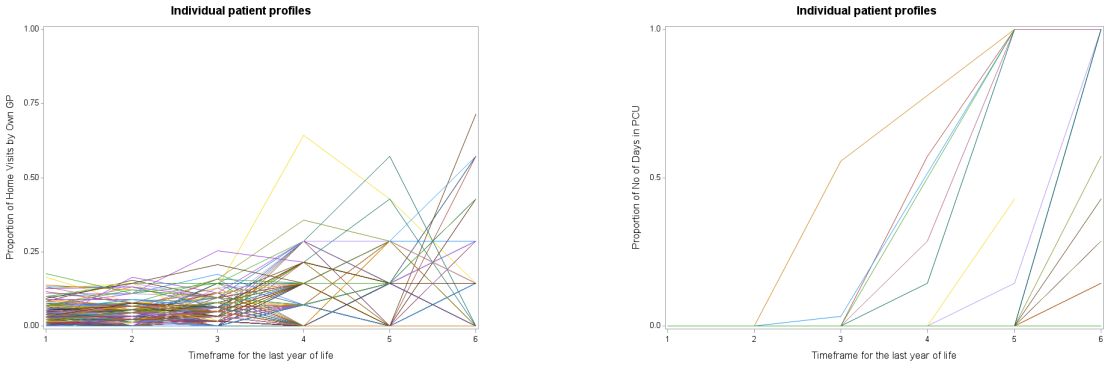

Figure 3: Individual Profiles For Home Visits and Days in PCU

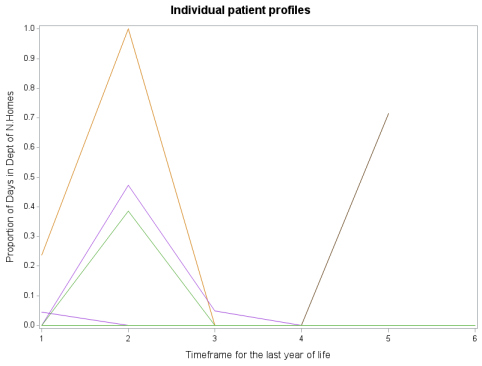

Figure 4: Individual Profiles For Days in Dept of N.Homes

3.2 Mean Profile Plots

Figure 5 shows the average profile of the proportion of number of days in Palliative Care Unit. It can be observed that there is an increase in the evolution of health care delivery (number of days in the Palliative Care Unit) as time diminishes , per cluster, per disease category and per social status or class of the patients. That is to say, patients tend to stay longer in the Palliative Care Unit as time decreases to zero. Specifically, cluster 4 had the highest evolution over time while cluster 2 had the least. Patients with cancer evolve far more than those without cancer and also patients with dementia evolved least as compared to those without dementia but with higher variability at time frame 6 than those without dementia. Similar trend was observed for patients in the social class, where patients with high social status evolved less (but with same variability) than those with normal social status. The average evolution of other health care delivery are shown in **APPENDIX B** where there is an

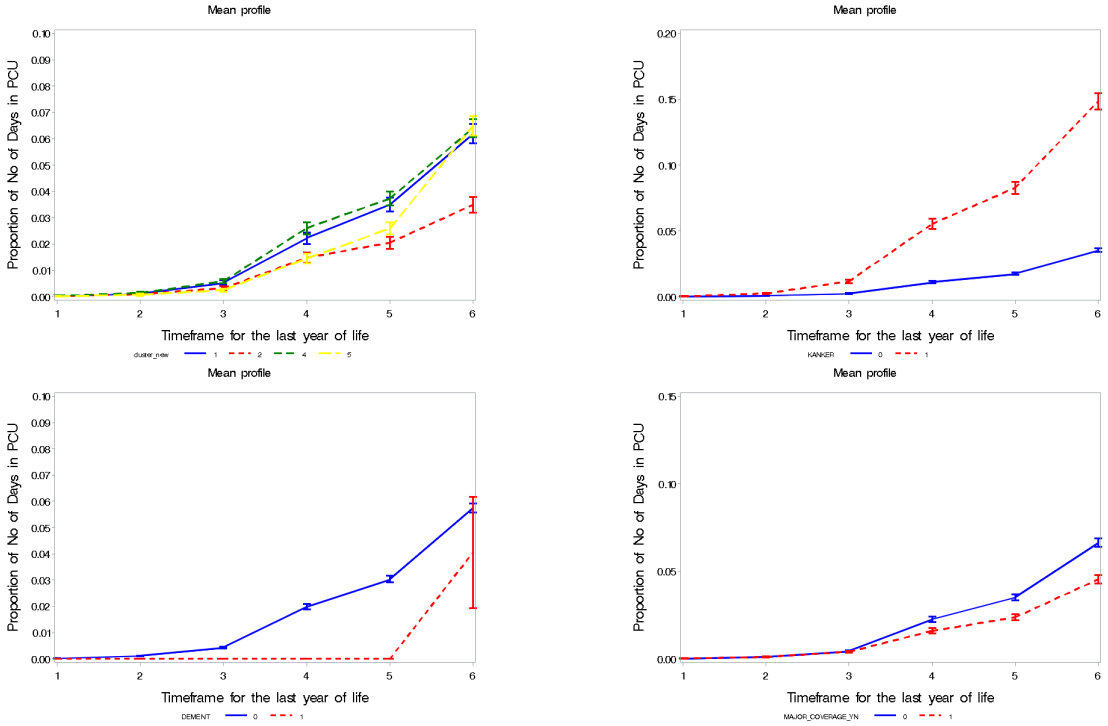

Figure 5: Mean Profile Plot for Proportion of Days in PCU

increase in the average evolution for proportion of hospitalisation days per cluster, per disease category and per social class(patients with high social class had less evolution than those in normal social class). For the proportion of days in nursing homes, the average evolution increases up to time frame 4 and then decreases, where patients with dementia had a very steady higher variability from time frame 1 to time frame 6. Similar trend in average evolution was observed for others health care delivery as seen in **APPENDIX B**. It is very apparent in all the average profiles that the variability tends to be low at the beginning but as time diminishes, the variability increases.

3.3 Variance Structure

Figure 6 shows the variance structure of the number of days in the Palliative Care Unit. It can be observed that there seems to be a linear evolution of variance over time. That is to say that this figure 6 suggests a constant variance function and hence linear models could be fitted. The variance structure of other responses are shown in **APPENDIX B** and they show the same trend as observed in Figure 6.

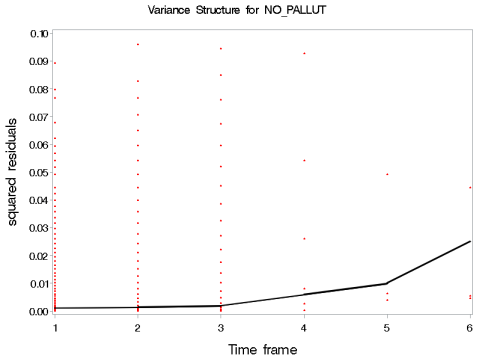

Figure 6: Variance Structure for Proportion of Days in PCU

3.4 Correlation of Response Variable

The correlation between the response variables were computed and the results are presented in Table 3. It can be observed that there seemed to be a very weak correlation between the response variables (since the pearson correlation coefficients are less than 0.5) and a high correlation within the response variables as expected as the patients were repeatedly measured. This explains why the response variables will be modeled independently and why models such as Poisson, Negative Binomial, zero-inflated poisson, zero-inflated negative binomial were modeled.

Table 3: Correlation Between Response Variable

	1	**2**	**3**	**4**	**5**	**6**	**7**
1	1	-0.00732	0.02048	0.00504	0.02354	0.02122	-0.01702
2	-0.00732	1	-0.00194	-0.00181	**0.28955**	**0.17883**	-0.05866
3	0.02048	-0.00194	1	-0.00426	0.01947	0.02995	-0.00192
4	0.00504	-0.00181	-0.00426	1	-0.03095	-0.04954	-0.04044
5	0.02354	**0.28955**	0.01947	-0.03095	1	**0.34296**	-0.14212
6	0.02122	**0.17883**	0.02995	-0.04954	**0.34296**	1	**0.4165**
7	-0.01702	-0.05866	-0.00192	-0.04044	-0.14212	**0.4165**	1

1 = NO_HOSPDAYS
2 = TV_P_DAYS
3 = NO_WZC_KORT
4 = NO_PALLU
5 = TV_DAYS
6 = HA_HB
7 = WZC

3.5 Statistical Analysis

Based on the results from exploratory data analysis, Poisson model and its extensions used in modeling count data were considered.

3.5.1 Poisson and Negative Binomial Models

The Standard Poisson and Negative Binomial models discussed in section **2.3.1** can be modeled respectively as: $y_i \sim Pois(\lambda_i)$, with $ln(\mu_i) = \alpha + \beta x_i$ and $y_i \sim Negbin(\mu_i, k)$, so that $log(\mu_i) = \eta_i = x_i^T\beta$, where the parameters $\mu = \alpha\beta$ and $k = 1/\alpha$ are the mean and the dispersion for the case of Negative Binomial model. These two models were fitted with same covariates of the data set, where responses were assumed to be independent.

3.5.2 The ZIP,ZINB and MMZI Models

The ZIP,ZINB,and MMZI can be fitted on our data by modeling μ_{ij} as:
$ln(\mu_{ij}) = \beta_0 + b_{1i} + \beta_1 * PV_{1i} + \beta_2 * PV_{2i} + \beta_3 * PV_{3i} + \beta_4 * PV_{4i} + \beta_5 * PV_{5i} + \beta_6 * PV_{6i} + \beta_7 * PV_{7i} + \beta_8 * PV_{8i} + \beta_9 * PV_{9i} + \beta_{10} * PV_{10i} + \beta_{11} * PV_{11i} + \beta_{12} * PV_{12i} + \beta_{13} * PV_{13i} + \beta_{14} * TIME_{ij} + \beta_{15} * PV_{15i} * TIME_{ij}$
and the zero-inflation probability as:
$logit(\pi_{ij}) = \gamma_0 + b_{2i} + \gamma_1 * PV_{1i} + \gamma_2 * PV_{2i} + \gamma_3 * PV_{3i} + \gamma_4 * PV_{4i} + \gamma_5 * PV_{5i} + \gamma_6 * PV_{6i} + \gamma_7 * PV_{7i} + \gamma_8 * PV_{8i} + \gamma_9 * PV_{9i} + \gamma_{10} * PV_{10i} + \gamma_{11} * PV_{11i} + \gamma_{12} * PV_{12i} + \gamma_{13} * PV_{13i} + \gamma_{14} * TIME_{ij}$,
where
$PV_1 = GMD$,$PV_2 = GP\_AGE05\_CAT$,$PV_3 = AGE05\_CAT$,$PV_4 = GMD$,$PV_5 = GMD$,$PV_6 = GMD$,$PV_6 = GMD$,$PV_7 = GMD$,$PV_8 = GMD$,$PV_9 = GMD$,$PV_{10} = GMD$,$PV_{11} = GMD$,$PV_{12} = GMD$,$PV_{13} = GMD$.
It should be noted that the ZIP and ZINB models have the same modeling procedure but differ at the level of their distributions (ie ZIP model, dist=zip and for ZINB, dist=zinb). The ZI(MEM) and MMZI were modeled using PROC NLMIXED after obtaining starting values from ZIP model and from GlIMMIX procedure .
Furthermore, the marginal mean model for the Poisson process is given as:
$ln(k_{ij}^m) = \beta_0 + \beta_1 * PV_{1i} + \beta_2 * PV_{2i} + \beta_3 * PV_{3i} + \beta_4 * PV_{4i} + \beta_5 * PV_{5i} + \beta_6 * PV_{6i} + \beta_7 * PV_{7i} + \beta_8 * PV_{8i} + \beta_9 * PV_{9i} + \beta_{10} * PV_{10i} + \beta_{11} * PV_{11i} + \beta_{12} * PV_{12i} + \beta_{13} * PV_{13i} + \beta_{14} * TIME_{ij} + \beta_{15} * PV_{15i} * TIME_{ij}$
The combined model assuming that the count are generated from Poisson-Normal-Gamma process has mean $\lambda_{ij}^c = \theta_{ij}k_{ij}$ with $\theta_{ij} \sim Gamma(\alpha, 1/\alpha)$. The marginal model for the zero-inflated probability is modeled as:
$F(\pi_{ij}^m) = \gamma_0 + \gamma_1 * PV_{1i} + \gamma_2 * PV_{2i} + \gamma_3 * PV_{3i} + \gamma_4 * PV_{4i} + \gamma_5 * PV_{5i} + \gamma_6 * PV_{6i} + \gamma_7 * PV_{7i} + \gamma_8 * PV_{8i} + \gamma_9 * PV_{9i} + \gamma_{10} * PV_{10i} + \gamma_{11} * PV_{11i} + \gamma_{12} * PV_{12i} + \gamma_{13} * PV_{13i} + \gamma_{14} * TIME_{ij}$,
where F(.) is the logit function and PV_{ni} are as defined above. Therefore, the corresponding conditional models have a normally distributed random intercept, b_{1i}, in the Poisson model and b_{2i}, in the binomial model such that $b_i \sim (b_{1i}, b_{2i})$ and are possibly correlated.

It should also be noted that the explanatory variables in the model fit were arrived at after model selection. The count parts in the final ZIP, ZINB, ZI(MEM) and MMZI models consisted of the same explanatory variables as in the Poisson and NB models. The zero-inflation parts of these models also consisted of the same explanatory variables but for the age and time interaction for the patient.

The results of the Poisson, Negative Binomial, Zero-Inflated Poisson,Zero-Inflated Negative Binomial,and MMZI for the response variable: the number of days in the Palliative Care Unit, are displayed in Table 4.

Table 4: Parameter Estimates with Standard Errors

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_o	0.470(0.0927)*	1.980(0.5258)*	1.964 (0.0960)*	2.047(0.2007)*	2.222(0.0567)*	1.999(0.2008)*
GMD	β_1	-0.156(0.0168)*	-0.438(0.0913)*	-0.045 (0.0173)*	-0.001(0.0372)	-0.016(0.0034)*	0.0001 (0.0372)
GP_AGE05_CAT	β_2	0.033 (0.0037)*	0.025(0.0191)	0.003 (0.0039)	0.001(0.0080)	0.005(0.0007)*	0.002(0.0080)
AGE05_CAT	β_3	-0.141(0.0038)*	-0.227(0.0237)*	-0.015(0.0040)*	-0.023(0.0085)	-0.0014(0.001)	-0.021(0.0085)
GENDER	β_4	-0.200(0.0143)*	-0.211(0.0736)*	-0.060(0.0143)*	-0.075(0.0289)	-0.055(0.0027)*	-0.074(0.0289)
FAM_SIZE	β_5	-0.179(0.0089)*	-0.263(0.0381)*	-0.040 (0.0083)*	-0.033(0.0165)	-0.046(0.0016)*	-0.032(0.0165)
PERIOD_D	β_6	-0.040(0.0028)*	-0.0447(0.0139)*	0.003(0.0028)	-0.002(0.0056)	-0.014(0.0005)*	-0.001 (0.0056)
MAJOR_COVERAGE_YN	β_7	0.013 (0.0153)	0.147(0.0788)	0.026(0.0154)	0.021(0.0315)	0.010(0.0029)*	0.022(0.0315)
CHRONZ_ATTEST	β_8	0.060 (0.0199)*	0.065 (0.0895)	-0.055(0.0199)*	-0.046(0.0394)	0.122(0.0036)*	-0.045(0.0394)
CHRONZ_FF	β_9	0.469 (0.0183)*	0.762(0.0954)*	0.142 (0.0185)*	0.119(0.0372)	0.089(0.0034)*	0.120(0.0372)
MAF	β_{10}	1.074(0.0193)*	1.378(0.0789)*	0.194 (0.0195)*	0.160(0.0373)	0.312(0.0033)*	0.161(0.0373)*
PF	β_{11}	0.491(0.0160)*	0.972(0.0935)*	-0.088(0.0156)*	-0.053(0.0314)	-0.124(0.0038)*	-0.054(0.0314)
KANKER	β_{12}	1.125(0.0151)*	1.309 (0.0858)*	0.076 (0.0145)*	0.067(0.0290)	-0.125(0.0034)*	0.067(0.0291)
DEMENT	β_{13}	-1.161(0.2296)*	-1.472(0.6256)*	-0.411 (0.2344)	-0.378(0.3798)	-0.096(0.0199)*	-0.398(0.3796)
TIME	β_{14}	-0.083(0.0075)*	-0.126 (0.0339)*	0.056 (0.0072)*	0.067(0.0278)	0.034(0.0009)*	0.070(0.0278)
AGE05_CAT*TIME	β_{15}	0.001 (0.0005)*	0.002(0.0021)	0.002(0.0005)*	0.003(0.0018)	0.001(0.0001)*	0.003(0.0018)
DEVIANCE	**G**	1.44	0.06				
DISPERSION	k		94.998(2.4601)*				
Inf_Intercept	γ_o			0.926(0.2668)*	0.833(0.2903)	-1.158(0.0869)*	0.877(0.2795)
Inf_GMD	γ_1			0.077(0.0530)	0.120(0.0564)	0.087(0.0174)*	0.110(0.0557)
Inf_GP_AGE05_CAT	γ_2			-0.032(0.0114)*	-0.030(0.0116)	0.0002(0.0036)	-0.030(0.0115)
Inf_AGE05_CAT	γ_3			0.143(0.0098)*	0.147(0.0098)*	0.089(0.0033)*	0.144(0.0010)*
Inf_GENDER	γ_4			0.168(0.0444)*	0.158(0.0446)	-0.126(0.0143)*	0.161(0.0444)
Inf_FAM_SIZE	γ_5			0.134(0.0265)*	0.121(0.0264)*	-0.042(0.0078)*	0.120(0.026)*
Inf_PERIOD_D	γ_6			0.054(0.0085)*	0.056(0.0086)*	0.050(0.0027)*	0.055(0.0086)*
Inf_MAJOR_COVERAGE_YN	γ_7			0.076(0.0477)	0.053(0.0481)	-0.142(0.0151)*	0.052(0.0478)
Inf_CHRONZ_ATTEST	γ_8			-0.090(0.0590)	-0.126(0.0594)	-0.075(0.0175)	-0.123(0.0592)
Inf_CHRONZ_FF	γ_9			-0.314(0.0562)*	-0.294(0.0566)*	-0.261(0.0188)*	-0.295(0.0564)*
Inf_MAF	γ_{10}			-0.908(0.0546)*	-0.928(0.0550)*	-1.001(0.0153)*	-0.925(0.0567)*
Inf_PF	γ_{11}			-0.517(0.0501)*	-0.525(0.0508)*	0.320(0.0197)*	-0.524(0.0509)*
Inf_KANKER	γ_{12}			-1.182(0.0465)*	-1.159(0.0467)*	-0.352(0.0182)*	-1.158(0.0501)*
Inf_DEMENT	γ_{13}			0.590(0.5093)	0.596(0.5076)	-0.275(0.1057)	0.590(0.5080)
Inf_TIME	γ_{14}			0.184(0.0064)*	0.187(0.0065)*	0.014(0.0008)*	0.185(0.0071)*
Var	$\sigma 2$					0.0101(0.0075)	
Std Deviation	σ_1				0.002(0.0018)		0.043(0.0223)
Std Deviation	σ_2				0.048(0.0380)		0.093(0.0398)
Alpha	α						0.320(0.0146)*
Tau	τ						-0.020(0.7160)
-2loglikelihood		147897.3	35866.5	36109	31145	36043	31154
AIC		147929.3	35900.5	36171	31213	36107	31224

$*$ = significant parameter estimates
$**$ = border line significant parameter estimates
Poisson= Poisson Model
NegBin= Negative Binomial Model
ZIP= Zero-Inflated Poisson Model
ZINB= Zero-Inflated Negative Binomial Model
ZI(MEM)= Zero-Inflated Mixed-Effects Model
MMZI= Marginalized Multilevel Zero-Inflated Combined Model

From Table 4, it can be observed that the ratio of the Deviance of the Poisson model to its degree of freedom was 1.44, which is greater than 1, confirming the presence of over-dispersion in the data. Therefore the Negative Binomial model was preferred which yielded a ratio of 0.06 with a log likelihood value of 35866.5 as opposed to that of Poisson model of 147897.3. It can also be observed from Table 4 that all the parameter estimates of the Poisson model are significantly associated with the number of days in the Palliative Care Unit unlike in the Negative Binomial model where DEMENT(Dementia) together with age and time interaction of the patients were not significantly associated with the number of days in the Palliative Care Unit. Over-dispersion actually was needed to be accounted for as can be seen from the dispersion parameter being significantly different from 0.

When overdispersion in the data is due to excess zeros, the Negative Binomial model is no longer a better choice. In such a situation like ours, the data were fitted using ZIP and ZINB models to account for overdispersion and the excess zero counts. Also, from Table 4, it can be seen clearly that ZINB model waq a better choice than Negative Binomial model in that their the $-2\times$loglikelihood and AIC are smaller in value. The dispersion parameter estimates of ZINB were also smaller as compared to that of NB model, indicating further that ZINB was a better choice.

Further, the AIC's made known of the preference of ZINB model to ZIP model in accounting for both the overdispersion phenomenon in the data and excess zero counts. It can also be observed that the parameter estimates in the count part of ZIP model were significant but not in the count part of ZINB model and some of the parameter estimates which were significant in the zero part of ZIP were not significant in ZINB model. This indicated that overdispersion was not accounted in the ZIP model but in the ZINB model.

As regards to KANKER(cancer), DEMENT(dementia) and MAJOR_COVERAGE_YN(social status), the probability of 0 day of stay per week in the Palliative Care Unit depends only on cancer since cancer was significantly different from zero. At cluster level, this probability depends on cancer and social status of the patients and marginally, it depends solely on cancer. That is to say, the odds of having 0 day of stay in Palliative Care Unit decreased by 31% for patients with cancer. At cluster level, these odds decreased by 70% and 86% for patients cancer and for patients in the higher social class of the patients, respectively. Marginally, the odds of having 0 day of stay in the Palliative Care Unit decreased by 30% for patients belonging to the cancer group.
For the count part, the number of days in the Palliative Care Unit was found to be related to cancer, dementia and social status only at cluster level (ie ZI(MEM) model), where the expected number of days in the Palliative Care Unit was increased by 1.01 times for patients belonging to higher social status , and the expected number of days in the Palliative Care Unit was decreased by 0.88(exp(-0.1254) = 0.88) and by 0.91 (exp(-0.0960) = 0.91) for patients in the cancer and dementia group, respectively. The results of number of days of stay in other settings are given in **APPENDIX C** and are interpreted in the same manner, where the ZINB model explains the specific effects , the ZI(MEM) model explains the effects at cluster level and MMZI gives the marginal interpretations.

Apparently, from Table 4, the estimates of the random effects appeared not to be significant but the effect of cancer, dementia and social status were significantly related to the number of days in the Palliative Care unit at cluster level. This actually calls for the application of statistical test to make a conclusive remark. To this effect, a mixture of χ^2-distributions was used, where model without random effect, model with only random intercept and model with random intercept and slope were considered for the test statistics; $\chi^2_{0:1}$ and $\chi^2_{1:2}$ were applied as : $P-Value = P(\chi^2_{0:1} > 66) = 0.5P(\chi^2_0 >$

$66) + 0.5P(\chi_1^2 > 66) = 2.220446e^{-16} < 0.05$
$P - Value = P(\chi_{1:2}^2 > 4889) = 0.5P(\chi_1^2 > 4,889) + 0.5P(\chi_2^2 > 4889) < 0.0001$. Thus it could be concluded that all the random effects had to stay in the models. These results suggest that there was significant cluster effects and that the Zero-Inflated mixed-effects models were plausible in accounting for the between- and within-patients variability in the health care delivery over time.

3.5.3 Model Diagnostic for ZINB Model

The estimated parameters of the ZINB model, AIC value and the test for overdispersion indicated a preference for the negative binomial version of the zero-inflated model(P-value ¡ 0.0001). The ZINB model also does a good job of estimating the proportion of zeros (exp(-1.1592)= 0.3137). There are studies on diagnostics and influence analysis for zero inflated models (Aldo, 2011). To explore the goodness of fit of ZINB model which merged as the better model for our analysis, the observed proportions as well as the average predicted count proportions for the number of days in the Palliative Care Unit from the Poisson, NB, ZIP and ZINB models were plotted as shown in Figure 6. From Figure 6, it can be seen that the Poisson model clearly underestimated the proportion of zero number of days in the Palliative Care Unit, while the other models (ZIP and ZINB) more accurate at zero. Further, the average predicted count probabilities for other responses are shown in **APPENDIX D**.

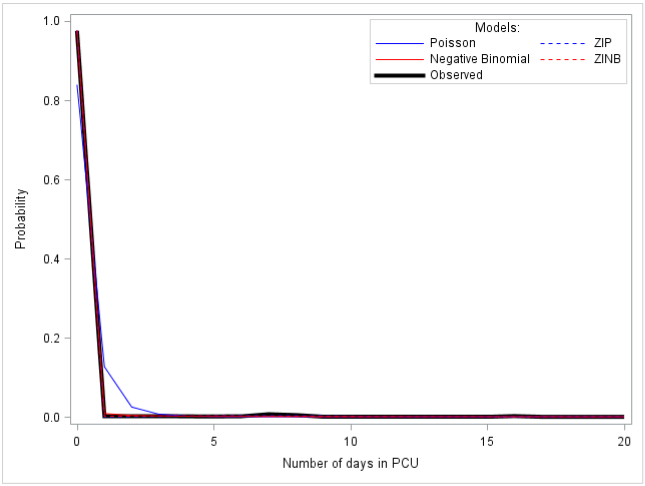

Figure 7: Average Predicted Count Probability

It can be observed also that the Poisson model clearly underestimated the proportion of zero number of days in the various settings, while the other models (ZIP and ZINB) more or quite accurate at zero.

4 DISCUSSION AND CONCLUSION

Implementation of the Care Pathway for Primary Palliative Care in 4 regions of Belgium was the topic of this project and it was aimed at investigating whether there are patterns of Health Care Delivery over time in the last year of life to be recognised overall, per cluster, per disease category and or per social status. The health care delivery in this study, comprises of the number of days in the different settings (hospital, nursing homes, pallaitive care) and number of home visits by a patient own GP. This constitutes a count data.

These count data are characterised by excess zeros, about 80% and thus Ordinary Poisson regression model cannot predict the expected number of days in the above mentioned settings. As such, Zero-Inflated Poisson Model(ZIP) was an alternative to analysed these data with excess zero counts. In practice, however, count data often over-dispersed and so Zero-Inflated Negative Binomial(ZINB) was applied, being a more appropriate model than the ZIP model and Negative Binomial model which only account for excess zero without over-dispersion and over-dispersion without excess zero counts respectively.

To account for within-patient variations or patient-specific effects, a random effects model was included. This was referred to as ZINB Mixed-effects model.Also, to account for the cluster effects, a Zero-Inflated mixed-effects model (ZI(MEM)) was considered and a Marginalizes Multilevel Zero-Inflated Combined models(a marginalized zero-inflated Poisson normal) were also fitted for marginal interpretation . However, according to Atkins and Gallop (2007), the inclusion of both fixed and random effects may complicate the likelihood equations, thus leading to non-convergence problem. In the analysis, the covariates FAM_SIZE consisted of 12 levels,. This actually posed a convergence problem with the WARNING MESSAGE: Execution error for observation 7 in the SAS log window. This problem was resolved by considering FAM_SIZE as a continuous variable. Despite this, SAS failed to provide valid estiamtes in PROC NLMIXED of ZI(PNG) and MMZI model for the responses TV_DAYS, TV_P_DAYS and NO_HOSPDAYS for WZC and WZC_KORT with WARNING MESSAGES: 1)The final Hessian matrix is full rank but has at least one negative eigenvalue. Second-order optimality condition violated. 2)The final Hessian matrix is not positive definite, and therefore the estimated covariance matrix is not full rank and may be unreliable. The variance of some parameter estimates is zero or some parameters are linearly related to other. Due to time constraint and SAS was taking more and more hours to run, more attempt could not be made to resolve the warning messages.

In all, ZINB, ZI(MEM) ,and MMZI were the best models considered for the number of days in different settings and for the number of home visits by own GP among others in estimating the parameters for the health care delivery. The ZINB model fitted by Proc NLMIXED is known to be valid under MAR mechanism. In these models, cancer and social status were seen to be significant both at count and at the zero parts for some of the models. Cluster effects were conspicuous and dementia was seen to be significant only at the count parts of some of the above mentioned models. Marginally, there were cancer, social status and cluster effects. Hence, there are patterns of health care delivery over time in the last year of life as recognised overall, per cluster, per disease category and or per social class.

It should also be noted that in this data set, there was one covariate , Age category of the GP (GP_AGE05_CAT), that had some of its values missing (1022 out of 102672 observations). To see if

this could affect the analysis, a Complete Case Analysis was applied and a model fitted. The results obtained were exactly the same as those of the model without the complete case analysis applied. These results are in line with the fact that generalised linear mixed models like in our case model missing data values. The results for these two models are shown in **APPENDIX E**

5 LIMITATION OF THE STUDY

The data consisted of many explanatory variables with some categorical variables having levels 5,6 and 12. This poses a lot of convergence problems at NLMIXED ROCEDURE which takes hours upon hours to converge. As such, in case of any error, to re-run it after correction which may not be perfect, will take another couple of hours to realised it or have the results. This entails time consumming for a limited duration of work . The explanatory variables were on the part too many and were all significant which provided no room for data reduction thus leading to over-parameterization and convergence becomes a problem.

In conclusion, the study revealed that there were patterns of health care delivery over time in the last year of life as recognised by overall, per cluster, per disease category and or per social status of the patients.

6 RECCOMENDATION

Emphasis should be laid on these types of models in the lessons of Longitudinal Data Analysis so that the techniques of handling PROC NLMIXED for the Zero-Inflated Poisson-Normal-Gamma models and the Marginalized Multilevel Zero-Inflated Combined Models can be well understood and taken care of against future challenges.

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APPENDIX A

6.1 Summary Statistics for Explanatory Variable

Table 5: Summary Statistics for Explanatory Variable

Variable	N	Mean	Std Dev	Variance	Min	Max
GMD	102672	0.795699	0.403192	0.162564	0	1
GP_AGE05_CAT	96540	11.65121	1.93038	3.726366	6	18
GENDER	102672	0.470605	0.499138	0.249138	0	1
AGE05_CAT	102672	16.55078	2.318427	5.375103	10	21
MAJOR_COVERAGE_YN	102672	0.432737	0.495458	0.245478	0	1
FAM_SIZE	102660	1.677323	0.942337	0.887998	1	12
MAF	102672	0.580353	0.493504	0.243546	0	1
CHRONZ_ATTEST	102672	0.541258	0.498297	0.2483	0	1
PERIOD_D	102672	16.9768	2.637776	6.957863	13	21
CHRONZ_FF	102672	0.277174	0.447605	0.200351	0	1
PF	102672	0.164271	0.370523	0.137287	0	1
KANKER	102672	0.194542	0.39585	0.156697	0	1
DEMENT	102672	0.003915	0.062451	0.0039	0	1
PLOD	102672	2.65159	1.003702	1.007419	1	5
DEPEND	102672	2.459561	1.859904	3.459245	0	5
TIME	102672	8.666667	8.95673	80.223	1	26

Figure 8: Histogram For For NO_HOSPDAYS and NO_PALLU

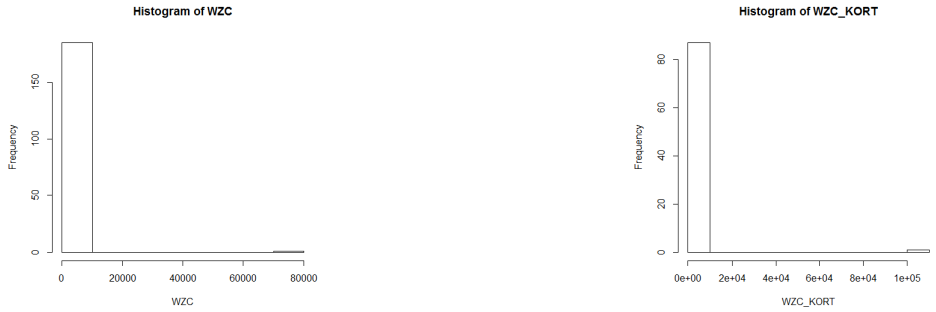


Figure 9: Histogram For For WZC and WZC_KORT

Figure 10: Histogram For WZC and WZC_KORT

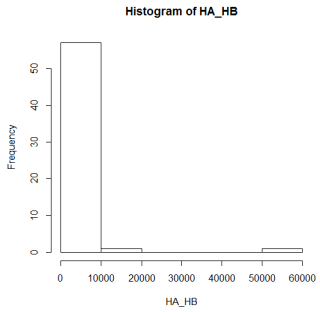


Figure 11: Histogram For HA_HB

6.2 Histograms of the Response Variable

APPENDIX B

6.3 Mean Profile Plots

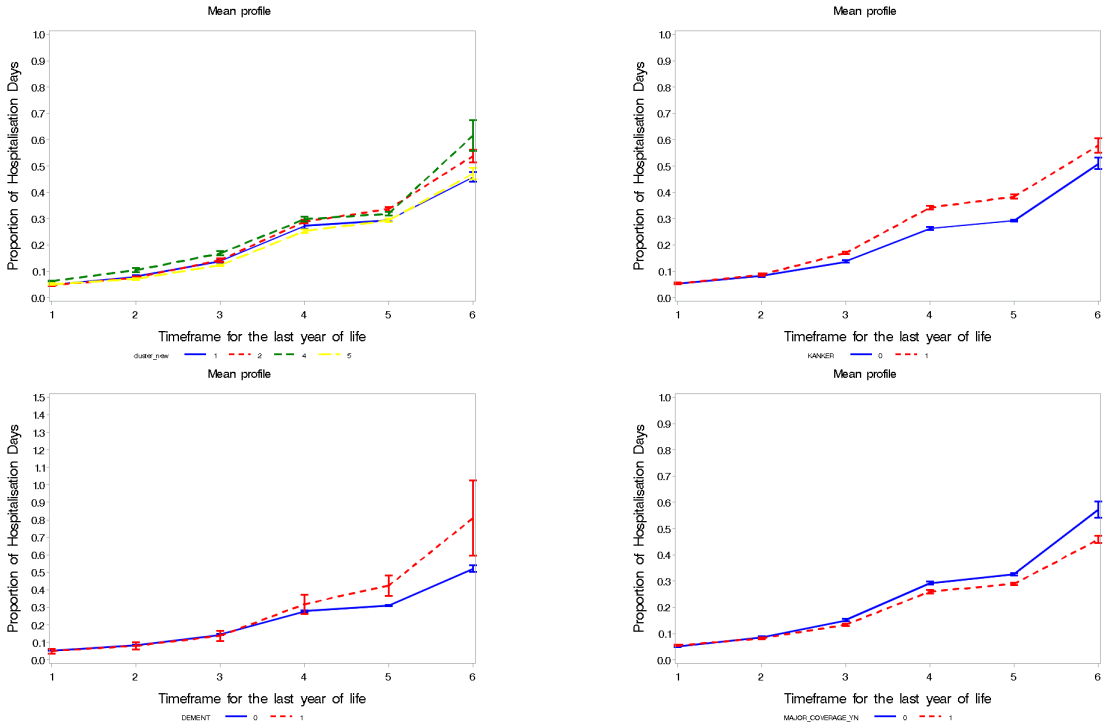


Figure 12: Mean Profile Plot For For Hospitalisation Days

APPENDIX C

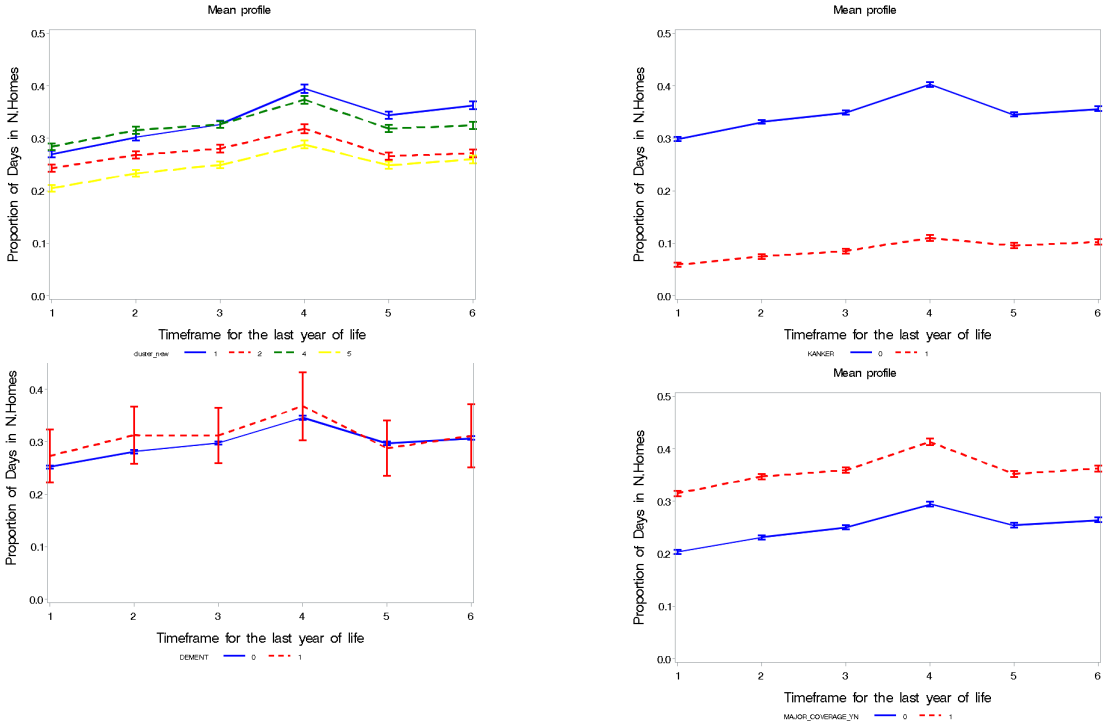


Figure 13: Mean Profile Plot For For Days in NHomes

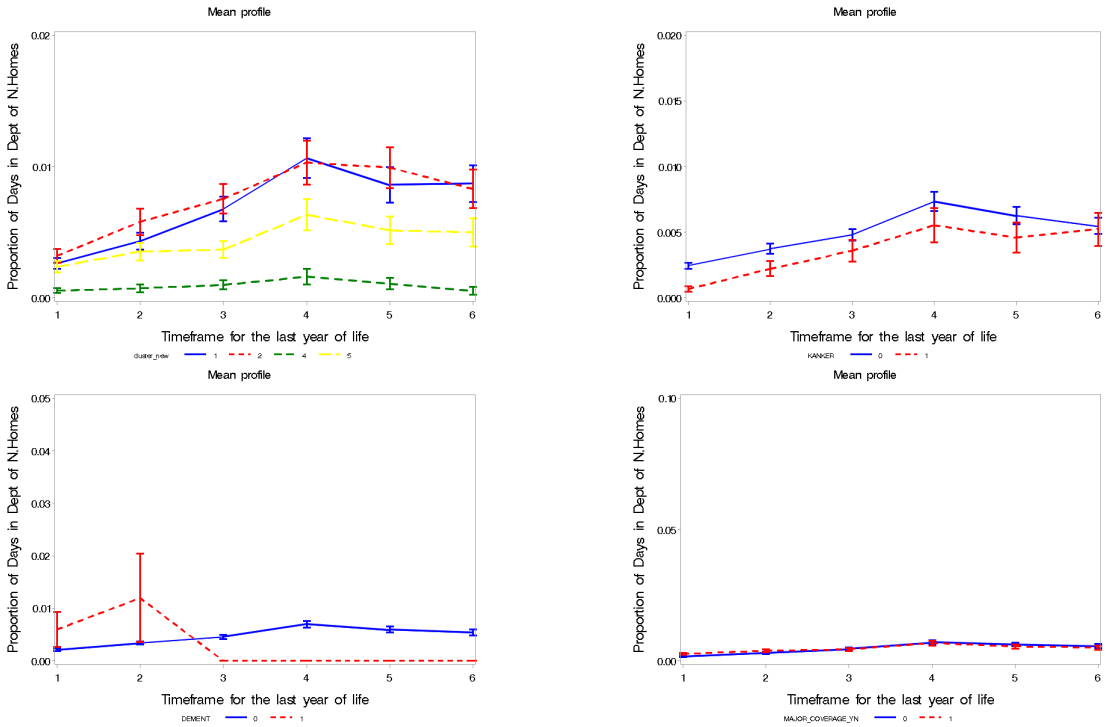


Figure 14: Mean Profile Plot For For Days in Dept of NHomes

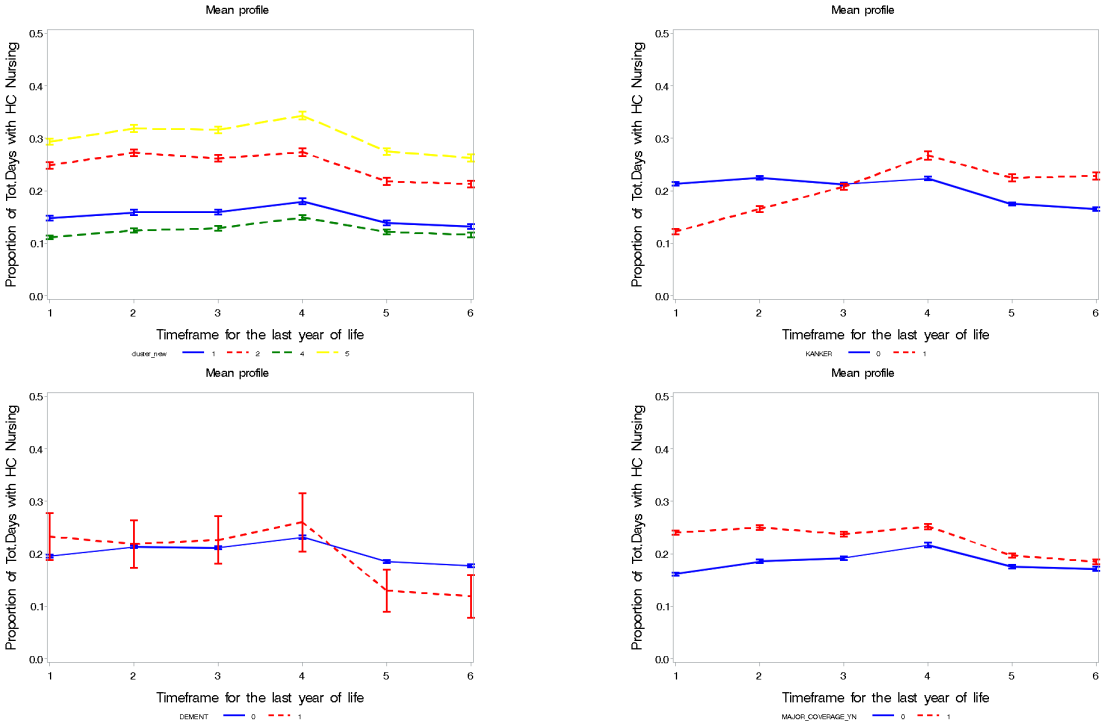


Figure 15: Mean Profile Plot For For TotDays with HC.Nursing

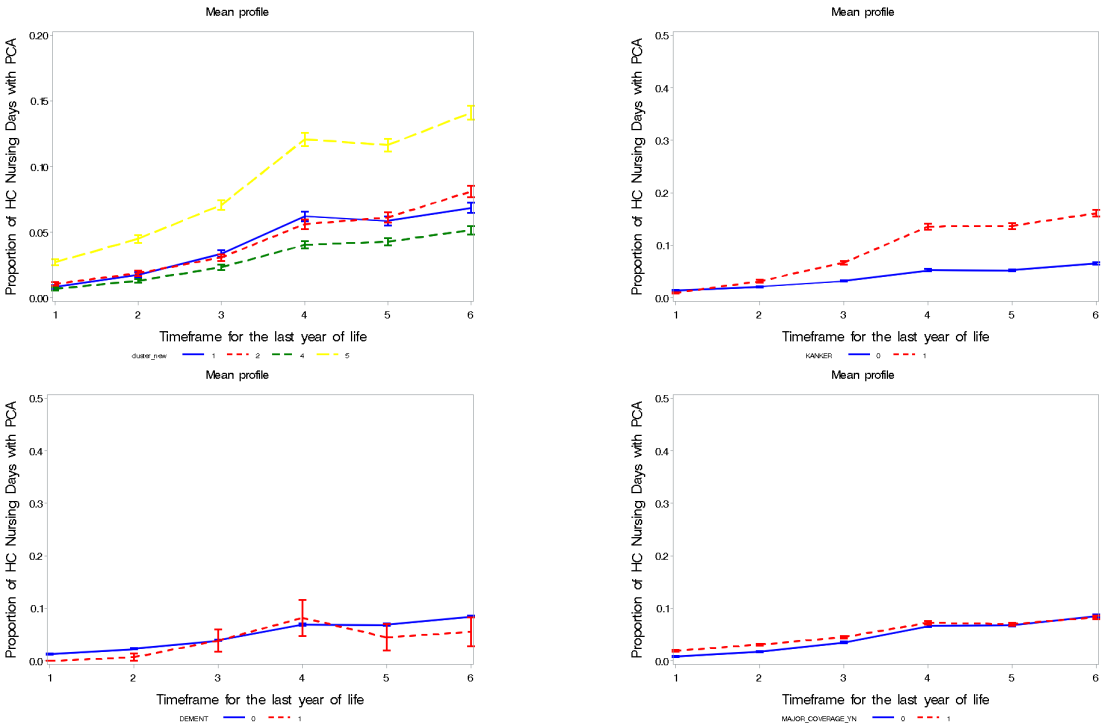


Figure 16: Mean Profile Plot For For HC Nursing Days with PCA

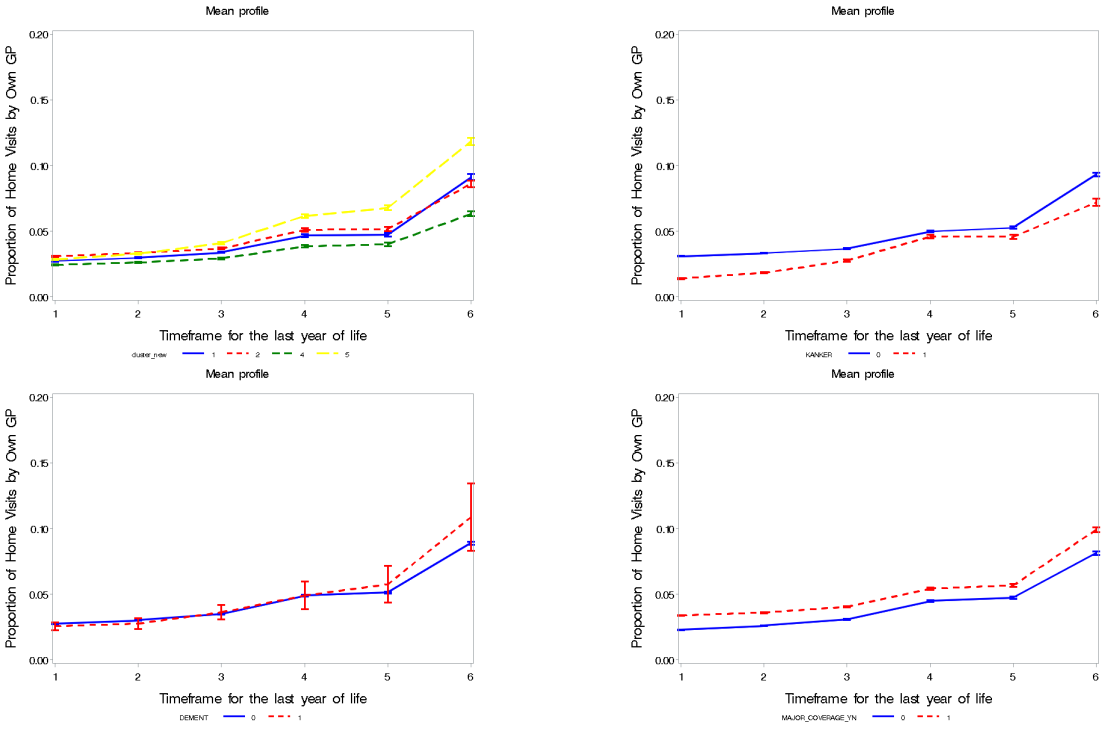


Figure 17: Mean Profile Plot For For Home Visits by own GP

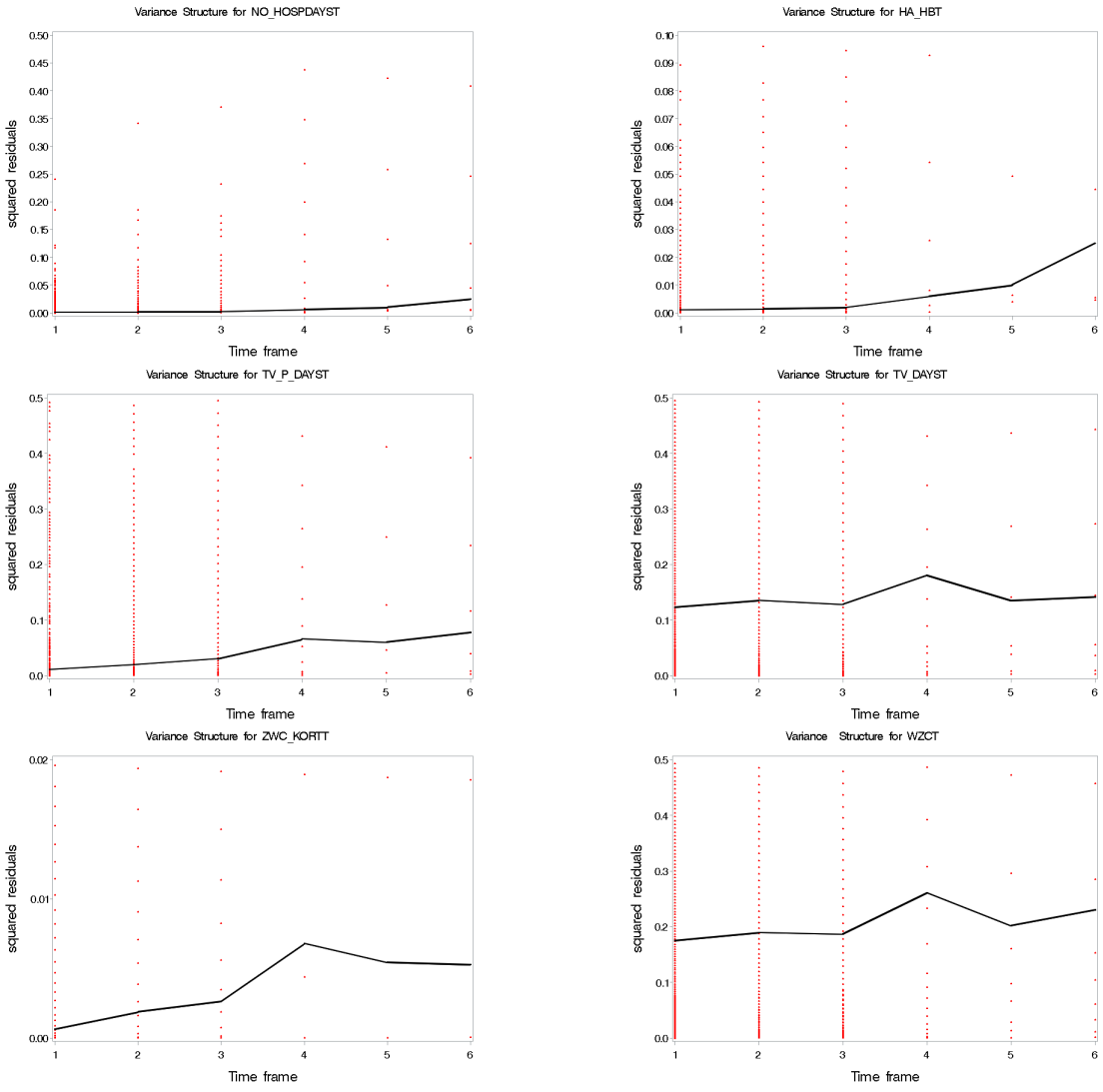


Figure 18: Variance Structures

Table 6: Parameter Estimates with Standard Errors For WZC

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_0	-0.833(0.0184)*	-3.450(0.1622)*	2.813(0.02039)*	2.319(0.0707)*	2.807(0.0213)*	0.00006(0.0001)*
GMD	β_1	0.134(0.0022)*	0.067(0.0249)*	0.017 (0.0022)*	0.009(0.0091)*	0.0217(0.00230)*	0.009(0.0091)
GP_AGE05_CAT	β_2	-0.004(0.0004)*	-0.015(0.0051)*	-0.001(0.0004)*	-0.0005(0.0017)	-0.001(0.0004)	-0.0006(0.0017)
AGE05_CAT	β_3	0.194(0.0009)*	0.299(0.0078)*	0.002 (0.0011)**	0.002(0.0035)	0.002(0.0011)	0.002(0.0035)
GENDER	β_4	-0.209(0.0018)*	-0.208(0.0202)*	-0.022(0.0018)*	-0.016(0.0074)	-0.021(0.0018)*	-0.016(0.0074)
FAM_SIZE	β_5	-0.538(0.0016)*	-0.419(0.0095)*	-0.031 0.0013)*	-0.019(0.0051)	-0.031(0.0013)*	-0.019(0.0051)
PERIOD_D	β_6	0.022(0.0003)*	0.035(0.0039)*	0.003 (0.0003)*	0.005(0.0013)	0.003(0.0003)*	0.0049(0.0013)
MAJOR_COVERAGE_YN	β_7	0.010(0.0018)*	0.208(0.0217)	-0.001(0.0018)*	-0.004(0.0075)	-0.002 (0.0018)*	-0.004(0.0074)
CHRONZ_ATTEST	β_8	0.119(0.0019)*	0.123(0.0250)*	-0.009(0.0019)*	-0.005(0.0081)	-0.007(0.0020)*	-0.004(0.0081)
CHRONZ_FF	β_9	-0.069(0.0024)*	0.095(0.0274)*	-0.0424 (0.0024)*	-0.007(0.0098)	-0.044(0.0024)*	-0.0077(0.0098)
MAF	β_{10}	-0.565(0.0018)*	-0.466(0.0215)*	-0.105 (0.0018)*	-0.112(0.0074)*	-0.107(0.0018)*	-0.112(0.0074)*
PF	β_{11}	-1.105(0.0042)*	-1.017(0.0285)*	-0.0525(0.0042)*	-0.052(0.0165)	-0.054(0.0042)*	-0.053(0.0165)
KANKER	β_{12}	-0.840(0.0037)*	0.905(0.0266)*	-0.06695 0.003662	-0.046(0.0142)	-0.066(0.0037)*	-0.046(0.0142)
DEMENT	β_{13}	-0.067(0.0118)*	0.005(0.1500)	-0.073 (0.0118)*	-0.046(0.0488)	-0.074(0.0119)*	-0.037(0.0489)
TIME	β_{14}	0.069(0.0008)*	0.069(0.0108)*	0.089 (0.0009)*	0.125(0.0053)*	0.089(0.0010)*	0.124(0.0053)*
AGE05_CAT*TIME	β_{15}	0.001(0.0000)*	0.0028(0.0006)*	0.0002(0.0001)*	0.0001(0.0003)	0.0002(0.00005)*	0.0002(0.0003)
DEVIANCE	**G**	29.71	0.67				
DISPERSION	k		8.638(0.0589)*		0.292(0.0027)*		
Inf_Intercept	γ_o			6.202(0.1177)*	6.247(0.1374)*	6.202(0.1177)*	6.222(0.1380)*
Inf_GMD	γ_1			-0.1976(0.0217)*	-0.253 0.0228)*	-0.198(0.0217)*	-0.252(0.0228)*
Inf_GP_AGE05_CAT	γ_2			0.007(0.0043)	0.013 (0.0044)	0.007(0.0043)	0.014(0.0044)
Inf_AGE05_CAT	γ_3			-0.391(0.0050)*	-0.392(0.0050)*	-0.391(0.0050)*	-0.392(0.0050)*
Inf_GENDER	γ_4			0.345(0.0174)*	0.334(0.0175)*	0.345(0.0174)*	0.335(0.0175)*
Inf_FAM_SIZE	γ_5			0.735(0.0132)*	0.716(0.0132)*	0.735(0.0132)*	0.716(0.0133)*
Inf_PERIOD_D	γ_6			-0.038(0.0032)*	-0.038 (0.00320)*	-0.038(0.0032)*	-0.038(0.0032)*
Inf_MAJOR_COVERAGE_YN	γ_7			-0.036(0.0181)*	-0.082(0.0185)*	-0.037(0.0181)	-0.080(0.0185)*
Inf_CHRONZ_ATTEST	γ_8			-0.324(0.021)*	-0.362 (0.0208)*	-0.324(0.0205)*	-0.363(0.0208)*
Inf_CHRONZ_FF	γ_9			0.112(0.0237)*	0.126(0.0239)*	0.111(0.0237)*	0.129(0.0239)*
Inf_MAF	γ_{10}			0.822(0.0178)*	0.821(0.0179)*	0.822(0.0178)*	0.822(0.0179)*
Inf_PF	γ_{11}			1.521(0.0327)*	1.511(0.0329)*	1.521(0.0328)*	1.512(0.0329)*
Inf_KANKER	γ_{12}			1.010(0.0287)*	1.019(0.0288)*	1.011(0.0287)*	1.017(0.0288)*
Inf_DEMENT	γ_{13}			0.048(0.1213)	0.089(0.1221)	0.133(0.1219)	0.066(0.1219)
Inf_TIME	γ_{14}			0.008(0.0009)*	0.009(0.0009)*	0.0084(0.0009)*	0.009(0.0009)*
Var	$\sigma 2$					0.00007(0.00006)	
Std Deviation	σ_1				-0.00008(0.0037)		-0.0003(0.0002)
Std Deviation	σ_2				0.139(0.0578)		0.141(0.0599)
Alpha	α						0.292(0.0027)*
Tau	τ						0.001(....)
-2loglikelihood		3028190.8	423936.4	608751	352055	608663	352055
AIC		3028222.8	423970.5	608813	352123	608727	352125

Table 7: Parameter Estimates with Standard Errors For WZC_KORT

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_0	-4.324(0.1429)*	-7.229(1.1567)*	3.228(0.1677)*	2.764(0.6612)**	3.103(0.1738)*	3.124(0.6664)*
GMD	β_1	-0.269(0.0176)*	-0.275(0.1723)	-0.197(0.01794)*	-0.203(0.0795)	-0.128(0.0194)*	-0.203(0.0798)
GP_AGE05_CAT	β_2	-0.048(0.0037)*	-0.030(0.0337)	-0.00299 (0.0036)	0.0007(0.0145)	-0.004(0.0036)	-0.002(0.0146)
AGE05_CAT	β_3	0.180(0.0071)*	0.260(0.0557)*	-0.0177(0.0085)*	-0.013(0.0329)	-0.015(0.0084)	-0.029(0.0332)
GENDER	β_4	-0.067(0.0157)*	-0.164(0.1393)	0.004344 (0.0156)	-0.001(0.0612)	0.026(0.0156)	-0.002(0.0612)
FAM_SIZE	β_5	-0.057(0.0095)*	-0.023(0.0846)	0.004 (0.0156)*	-0.072(0.0397)	-0.068(0.0100)*	-0.075(0.0397)
PERIOD_D	β_6	-0.036(0.0028)*	0.015(0.0262)	-0.012 (0.0029)*	-0.003(0.0115)	-0.008(0.0029)	-0.005(0.0115)
MAJOR_COVERAGE_YN	β_7	0.102(0.0161)*	0.034(0.1530)	0.0670(0.0165)*	0.037(0.0671)	0.044(0.0168)	0.036(0.0673)
CHRONZ_ATTEST	β_8	0.243(0.0183)*	0.287(0.1826)	-0.101 (0.0191)*	-0.038(0.0794)	-0.110(0.0196)*	-0.044(0.0795)
CHRONZ_FF	β_9	-0.0831(0.0204)*	-0.323(0.1891)	-0.199 (0.0206)*	-0.252(0.0806)	-0.193(0.0206)*	-0.252(0.0806)
MAF	β_{10}	0.562(0.0168)*	0.719(0.1498)*	0.088 (0.0172)*	0.084(0.0694)	0.062(0.0173)	0.079(0.0696)
PF	β_{11}	-0.659(0.0283)*	-0.573(0.2035)*	-0.178(0.0291)*	-0.119(0.1098)	-0.152(0.0293)*	-0.120(0.1098)
KANKER	β_{12}	-0.240(0.0242)*	-0.001(0.1928)*	0.115(0.0247)*	0.164(0.0972)	0.125(0.0248)*	0.157(0.0973)
DEMENT	β_{13}	0.471(0.0831)*	-0.067(1.0409)	-0.203 (0.0841)*	0.082(0.3811)	-0.275(0.0846)*	-0.112(0.3520)
TIME	β_{14}	-0.0009(0.0070)*	0.065(0.0758)	0.026 (0.0083)*	0.051(0.0409)	0.021(0.0082)	0.035(0.0409)
AGE05_CAT*TIME	β_{15}	0.004(0.0004)*	0.002(0.0045)	0.001(0.0005)*	0.0007(0.0023)	0.002(0.0005)*	0.002(0.0023)
DEVIANCE	**G**	1.83	0.02				
DISPERSION	k		410.465 (15.6172)*		0.695(0.0411)*		
Inf_Intercept	γ_o			8.348(0.4789)*	8.728(0.6492)*	8.351(0.4789)*	8.274(0.8738)*
Inf_GMD	γ_1			0.091(0.0841)	0.236(0.0909)	0.093(0.0841)	0.235(0.0879)
Inf_GP_AGE05_CAT	γ_2			0.051(0.0169)*	0.025 (0.0169)	0.051(0.0169)**	0.023(0.0163)
Inf_AGE05_CAT	γ_3			-0.231(0.0199)*	-0.239(0.0202)*	-0.231(0.0199)*	-0.229(0.0261)*
Inf_GENDER	γ_4			-0.231(0.0199)	0.086(0.0713)	0.055(0.0709)*	0.083(0.0686)
Inf_FAM_SIZE	γ_5			0.011(0.0412)	0.028(0.0428)	0.011(0.0413)	0.026(0.0410)
Inf_PERIOD_D	γ_6			0.011(0.0413)	0.010 (0.0129)	0.013(0.0129)	0.010(0.0124)
Inf_MAJOR_COVERAGE_YN	γ_7			0.005(0.0734)	0.097 (0.0747)	0.004(0.0734)	0.094(0.0719)
Inf_CHRONZ_ATTEST	γ_8			-0.317(0.0847)*	-0.235(0.0857)	-0.316(0.0847)*	-0.233(0.0844)
Inf_CHRONZ_FF	γ_9			-0.008(0.0907)	-0.091(0.0919)	-0.008(0.0907)	-0.084(0.0881)
Inf_MAF	γ_{10}			-0.635(0.0780)*	-0.639 (0.0791)*	-0.636(0.0780)*	-0.617(0.0896)*
Inf_PF	γ_{11}			0.511(0.1176)*	0.501(0.1190)**	0.510(0.1176)*	0.479(0.1195)**
Inf_KANKER	γ_{12}			0.217(0.1069)*	0.250(0.1077)	0.218(0.1069)	0.239(0.1050)
Inf_DEMENT	γ_{13}			-0.371(0.394)	-0.245(0.4203)	-0.268(0.4138)	-0.308(0.3900)
Inf_TIME	γ_{14}			-0.021(0.0034)	-0.019(0.0035)*	-0.021(0.0034)*	-0.018(0.0036)*
Var	$\sigma 2$					0.0098(0.0071)	
Std Deviation	σ_1				0.071(0.0410)		0.073 (0.0426)
Std Deviation	σ_2				0.857(0.2958)		0.319 (0.1183)
Alpha(Dispersion)	α						0.695(0.0411)*
Tau	τ						0.0290.9869)
-2loglikelihood		180512.8	1793.0	26215	16717	26024	16717
AIC		180544.9	17964.3	26277	16785	26088	16787

Table 8: Parameter Estimates with Standard Errors For HA_HB

EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
INTERCEPT	β_0	-1.969(0.0430)*	-2.178(0.0734)*	0.384 (0.0502)*	0.006(0.0802)	0.382(0.05156)*	0.313(1.5032)
GMD	β_1	0.258 (0.0064)*	0.249(0.0120)*	0.212 0.0070)*	0.235(0.0122)*	0.221(0.0073)*	0.237(0.0124)*
GP_AGE05_CAT	β_2	0.013(0.0012)*	0.012 (0.0024)*	0.016 (0.0013)*	0.015(0.0023)*	0.016(0.0013)*	0.015(0.0023)*
AGE05_CAT	β_3	0.088(0.0021)*	0.092(0.0034)*	-0.013 (0.0025)*	-0.012(0.0037)	-0.013(0.0025)*	-0.012(0.0038)
GENDER	β_4	-0.111(0.0049)*	-0.099(0.0095)*	-0.037 (0.0052)*	-0.03285(0.0091)	-0.037 (0.0052)*	-0.031(0.0092)
FAM_SIZE	β_5	-0.071(0.0029)*	-0.067(0.0054)*	-0.044 (0.0031)*	-0.045(0.0053)*	-0.047(0.0031)*	-0.044(0.0054)*
PERIOD _D	β_6	-0.006(0.0009)*	0.009(0.0017)*	-0.005(0.0009)*	-0.008 (0.0016)*	-0.005 (0.00093)*	-0.0083 (0.0016)*
MAJOR_COVERAGE_YN	β_7	0.209(0.0049)*	0.197(0.0098)*	0.133(0.0052)*	0.111 (0.0095)*	0.127(0.0053)*	0.113 (0.0095)*
CHRONZ_ATTEST	β_8	0.094(0.0056)*	0.126 (0.0113)*	0.022(0.0060)*	0.034(0.0107)	0.021(0.0061)*	0.033(0.0108)
CHRONZ_FF	β_9	0.172(0.0062)*	0.129 (0.0125)*	0.133(0.0066)*	0.103(0.0118)*	0.132(0.0066)*	0.102(0.0119)*
MAF	β_10	-0.103(0.0050)*	-0.126(0.0099)*	-0.036(0.0053)*	-0.054(0.0095)*	-0.039(0.0053)*	-0.053 (0.0096)*
PF	β_11	0.330(0.0062)*	0.574(0.0130)*	0.191(0.0067)*	0.302(0.0126)*	0.189(0.0068)*	0.318(0.0129)*
KANKER	β_12	-0.346(0.0072)*	-0.317(0.0130)*	-0.153(0.0078)*	-0.124(0.0135)*	-0.150(0.0078)*	-0.121 (0.0136)*
DEMENT	β_13	-0.172(0.0364)*	-0.083(0.0704)	-0.159(0.0389)*	-0.129(0.0676)	-0.159(0.0390)*	-0.109(0.0680)
TIME	β_14	0.034(0.0019)*	0.022(0.0040)*	0.014(0.0022)*	0.014(0.0040)	0.013(0.0022)*	0.016(0.0041)**
AGE05_CAT	β_15	0.003(0.0001)*	0.004(0.0002)*	0.003(0.0001)*	0.004(0.0002)*	0.003(0.0001)*	0.004(0.0002)*
DEVIANCE	G	2.65	0.98				
DISPERSION	k		1.156(0.0102)*		0.489(0.0075)*		
In_INTERCEPT	γ_0			4.449(0.1064)*	4.904(0.3574)*	4.449(0.1064)*	9.457(0.8649)*
In_GMD	γ_1			4.449(0.1062)*	-0.113(0.0344)	-0.109(0.0216)*	-0.148(0.0434)
In_GP_AGE05_CAT	γ_2			-0.110(0.0215)*	0.014 0.0069)	0.014(0.0043)*	0.019(0.0083)
In_AGE05_CAT	γ_3			-0.265(0.0041)*	-0.361 (0.0063)*	-0.265(0.0042)*	-0.448(0.0270)*
In_GENDER	γ_4			0.217(0.0169)*	0.343(0.0257)*	0.217(0.0169)*	0.413(0.0383)*
In_FAM_SIZE	γ_5			0.056(0.0096)*	0.0947(0.0138)*	0.055(0.0096)*	0.125(0.0187)
In_PERIOD _D	γ_6			-0.004(0.0032)	-0.010(0.0048)	-0.003(0.0032)	-0.013(0.0057)
In_MAJOR_COVERAGE_YN	γ_7			-0.174(0.0178)*	-0.236 (0.0281)*	-0.175(0.0179)*	-0.238(0.0344)*
In_CHRONZ_ATTEST	γ_8			-0.280(0.0210)*	-0.363 (0.0328)*	-0.280(0.0210)*	-0.423(0.0445)*
In_CHRONZ_FF	γ_9			-0.002(0.0227)	-0.030(0.0348)	-0.002(0.0227)	-0.049(0.0418)
In_MAF	γ_10			0.354(0.0179)*	0.485(0.0278)*	0.353(0.0180)*	0.567(0.0447)*
In_PF	γ_11			-0.748(0.0241)*	-0.865(0.0380)*	-0.748(0.0241)*	-0.866(0.0547)*
In_KANKER	γ_12			0.463(0.0217)*	0.580(0.0303)*	0.463(0.0218)*	0.712(0.0552)*
In_DEMENT	γ_13			0.123(0.1325)	0.115(0.2239)	0.123(0.1327)	0.208(0.2438)
In_TIME	γ_14			-0.064(0.0010)*	-0.038 (0.0016)*	-0.064(0.0010)*	-0.041(0.0026)*
Var	σ^2					0.0005(0.0004)	
Std Deviation	σ_1				0.018(0.0079)		
Std Deviation	σ_2				0.482(0.2752)		
Alpha(Dispersion)	α						0.501(0.0079)*
Tau	τ						-0.989(0.0205)*
log(Stdev1)	σ_1						-2.429(0.7885)
log(Stddev2)	σ_2						0.557(0.3703)
-2Log Likelihood		401195.08	319987.46	341477	312234	341407	312107
AIC		401227.08	319993.73	341539	312302	341471	312181

Table 9: Parameter Estimates with Standard Errors For NO_HOSPDAYS

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_o	1.748(0.0201)*	1.999(0.0961)*	2.221 (0.0203)*	1.200(0.0749)*	2.222(0.0567)*	
GMD	β_1	-0.080(0.0032)*	-0.070(0.0208)*	-0.043(0.0032)*	-0.014(0.0139)*	-0.016(0.0034)*	
GP_AGE05_CAT	β_2	0.011(0.0007)*	0.011(0.0042)*	0.009(0.0007)*	0.011(0.0027)**	0.005(0.0007)*	
AGE05_CAT	β_3	-0.036(0.0009)*	-0.048(0.0056)*	0.00006 (0.0009)	-0.0006(0.00357)	-0.001(0.0010)	
GENDER	β_4	0.012(0.0027)*	0.056(0.0170)*	-0.059(0.0027)*	-0.052(0.0109)*	-0.055(0.0027)	
FAM_SIZE	β_5	-0.046(0.0016)*	-0.019(0.0090)*	-0.055 (0.0016)*	-0.045(0.0056)*	-0.046(0.0016)*	
PERIOD_D	β_6	-0.036(0.0005)*	-0.042(0.0031)*	-0.013 (0.0005)*	-0.014(0.0020)*	-0.014(0.0005)*	
MAJOR_COVERAGE_YN	β_7	0.069(0.0029)*	0.073(0.0179)*	-0.012(0.0029)*	-0.0270(0.0116)	0.010(0.0029*	
CHRONZ_ATTEST	β_8	0.217(0.0036)*	0.049(0.0207)*	0.100 (0.0036)*	0.052(0.0141)	0.122(0.0036)*	
CHRONZ_FF	β_9	0.290(0.0035)*	0.268(0.0226)*	0.101 (0.0034)*	0.051(0.0143)	0.088(0.0034)*	
MAF	β_{10}	0.868(0.0033)*	0.932(0.0175)*	0.305(0.0033)*	0.328(0.0125)*	0.312(0.0033)*	
PF	β_{11}	-0.203(0.0038)*	-0.221(0.0231)*	-0.139 (0.0038)*	-0.157(0.0151)*	-0.124(0.0038)*	
KANKER	β_{12}	0.029(0.0034)*	0.127(0.0219)*	-0.121(0.0034)*	-0.079(0.0132)*	-0.125(0.0034)*	
DEMENT	β_{13}	0.063(0.0199)*	0.032(0.1277)	-0.097 (0.0199)*	-0.052(0.0784)	-0.096(0.0199)*	
TIME	β_{14}	0.044(0.0009)*	0.046(0.0076)*	0.035 (0.0009)*	0.045 (0.0048)*	0.034(0.0009)*	
AGE05_CAT*TIME	β_{15}	-0.0002(0.0001)*	0.0001(0.0005)	0.001(0.00006)*	0.001(0.0003)	0.0007(0.00005)*	
DEVIANCE	**G**	16.76	0.78				
DISPERSION	k^{-1}		6.201(0.0396)*		0.996(0.0117)*		
Inf_Intercept	γ_o			-1.158(0.0869)*	-1.468 (0.0963)*	-1.158(0.0869)*	
Inf_GMD	γ_1			0.087(0.0174)*	0.093 (0.01917)*	0.087(0.0173)*	
Inf_GP_AGE05_CAT	γ_2			0.0002(0.0036)*	0.002(0.0039)	0.0002(0.0036)	
Inf_AGE05_CAT	γ_3			0.089(0.0033)*	0.097(0.0036)*	0.089(0.0033)*	
Inf_GENDER	γ_4			-0.126(0.0142)*	-0.143 (0.0156)*	-0.126(0.0143)*	
Inf_FAM_SIZE	γ_5			-0.042(0.0078)*	-0.052 (0.0087)*	-0.042(0.0078)	
Inf_PERIOD_D	γ_6			0.050(0.0027)*	0.050 (0.0029)*	0.050(0.0027)*	
Inf_MAJOR_COVERAGE_YN	γ_7			-0.142(0.0150)*	-0.163(0.0165)*	-0.142(0.0150)*	
Inf_CHRONZ_ATTEST	γ_8			-0.075(0.0175)*	-0.074 (0.0189)	-0.075(0.0175)*	
Inf_CHRONZ_FF	γ_9			-0.261(0.0188)*	-0.287 0.0207)*	-0.261(0.0188)*	
Inf_MAF	γ_{10}			-1.0006 (0.0153)*	-1.011 (0.0165)*	-1.0005(0.0153)*	
Inf_PF	γ_{11}			0.320 (0.0197)*	0.292 (0.0218)*	0.320(0.0197)*	
Inf_KANKER	γ_{12}			-0.352(0.0182)*	-0.390 (0.0203)*	-0.352(0.0182)*	
Inf_DEMENT	γ_{13}			-0.275 (0.1057)*	–0.291(0.1162)	-0.275(0.1057)	
Inf_TIME	γ_{14}			0.014 (0.0008)*	0.022 0.0008)*	0.0143(0.0007)*	
Var	$\sigma 2$					0.010(0.0075)	
Std Deviation	σ_1				0.012(0.0140)		
Std Deviation	σ_2				-111E-14 (0.0001)		
Alpha	α						
Tau	τ						
-2loglikelihood		1772232.6	411030.6	924694	390586	918990	
AIC		1772264.6	411064.6	924756	390654	919054	

Table 10: Parameter Estimates with Standard Errors For TV_P_DAYS

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_0	-2.647(0.0395)*	-6.446(0.3349)*	2.260(0.0400)*	1.796(0.1522)*	2.270(0.0423)*	
GMD	β_1	0.088(0.0071)*	0.142(0.0575)*	0.026 (0.0072)*	0.050(0.0292)	0.023(0.0076)**	
GP_AGE05_CAT	β_2	-0.009(0.0013)*	0.040(0.0119)*	-0.001(0.0013)	-0.002(0.0051)	-0.002(0.0013)	
AGE05_CAT	β_3	0.002(0.0018)	0.018(0.0157)*	0.016(0.0018)*	0.016(0.0065)	0.0169(0.0018)*	
GENDER	β_4	-0.119(0.0053)*	-0.300(0.0457)*	-0.032(0.0053)*	-0.042(0.0211)	-0.030(0.0053)*	
FAM_SIZE	β_5	0.154(0.0022)*	0.631(0.0336)*	-0.001 (0.0025)	0.0007(0.0108)	-0.003(0.0025)*	
PERIOD_D	β_6	0.018(0.0010)*	0.028(0.0087)*	0.005(0.0010)*	0.0012(0.0041)	0.005(0.0010)*	
MAJOR_COVERAGE_YN	β_7	0.371(0.0056)*	0.421(0.0470)*	0.070(0.0056)*	0.046(0.0224)	0.061(0.0056)*	
CHRONZ_ATTEST	β_8	1.293(0.0090)*	2.258(0.0585)*	0.138(0.0090)*	0.082(0.0318)	0.131(0.0090)*	
CHRONZ_FF	β_9	0.122(0.0061)*	-0.279(0.0607)*	-0.007 (0.0061)*	0.025(0.0244)	-0.008(0.0062)*	
MAF	β_{10}	-0.227(0.0057)*	-0.197(0.0496)*	-0.048 (0.0058)*	-0.059(0.0230)	-0.046(0.0058)*	
PF	β_{11}	2.407(0.0062)*	4.020(0.0637)*	-0.377 (0.0065)*	-0.197(0.0342)*	-0.378 (0.0065)*	
KANKER	β_{12}	-0.119(0.0062)*	-0.323(0.0604)*	-0.090(0.0063)*	-0.027(0.0229)	-0.085(0.0062)*	
DEMENT	β_{13}	-0.625(0.0552)*	-2.243(0.3962)*	-0.056(0.0553)	0.037(0.1820)	-0.051(0.0553)*	
TIME	β_{14}	-0.032(0.0018)*	0.049(0.0203)*	0.098 (0.0018)*	0.158 (0.0134)*	0.098(0.0018)*	
AGE05_CAT*TIME	β_{15}	0.005(0.0001)*	0.004(0.0012)*	-0.0003(0.0001)*	-0.001(0.0008)	-0.0003(0.0001)*	
DEVIANCE	**G**	7.39	0.161				
DISPERSION	k		35.469(0.5423)*		0.573(0.0169)*		
Inf_Intercept	γ_o			5.894(0.2072)*	5.785(0.2287)*	5.904(0.2073)*	
Inf_GMD	γ_1			-0.060(0.0430)	-0.024 (0.0471)	-0.057(0.0430)*	
Inf_GP_AGE05_CAT	γ_2			0.009(0.0081)	0.0079(0.0083)	0.009(0.0081)	
Inf_AGE05_CAT	γ_3			-0.038(0.0074)*	-0.037 (0.0077)*	-0.038(0.0074)*	
Inf_GENDER	γ_4			0.068(0.0328)*	0.069(0.0338)	0.070(0.0328)*	
Inf_FAM_SIZE	γ_5			-0.144(0.0160)*	-0.141(0.0167)*	-0.144(0.0160)*	
Inf_PERIOD_D	γ_6			-0.017(0.0064)*	-0.014 (0.0065)	-0.017(0.0064)	
Inf_MAJOR_COVERAGE_YN	γ_7			-0.258(0.0344)*	-0.249(0.0357)*	-0.255(0.0344)*	
Inf_CHRONZ_ATTEST	γ_8			-0.913(0.0448)*	-0.913(0.0462)*	-0.914(0.0448)*	
Inf_CHRONZ_FF	γ_9			-0.072(0.0385)	-0.057(0.0399)	-0.072(0.0385)	
Inf_MAF	γ_{10}			0.211(0.0352)*	0.177(0.0363)*	0.213(0.0352)*	
Inf_PF	γ_{11}			-4.044(0.0436)*	-4.072(0.0444)*	-4.045(0.0437)*	
Inf_KANKER	γ_{12}			-0.086(0.0355)*	-0.086(0.0367)	-0.089(0.0355)	
Inf_DEMENT	γ_{13}			-0.095(0.2679)	-0.076(0.2744)	0.133(0.2781)	
Inf_TIME	γ_{14}			0.081(0.0023)*	0.087(0.0023)*	0.081(0.0023)*	
Var	$\sigma 2$					0.0008(0.0006)	
Std Deviation	σ_1				-111E-14(0.0004)		
Std Deviation	σ_2				0.026(0.0191)		
Alpha	α						
Tau	τ						
-2loglikelihood		740309.49	92583.90	124446	71429	124359	
AIC		740341.49	92617.90	124508	71497	124423	

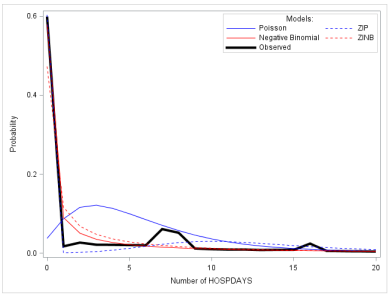
Table 11: Parameter Estimates with Standard Errors For TV_DAYS

		MODEL					
EFFECT	**Parms**	**Poisson**	**NegBin**	**ZIP**	**ZINB**	**ZI(MEM)**	**MMZI**
Intercept	β_0	0.193(0.0168)*	-0.149(0.1665)	1.945 (0.01728)*	1.593(0.1014)*	1.881(0.0574)*	
GMD	β_1	0.020(0.0024)*	-0.0009(0.0266)	0.04845 (0.0024)*	0.035(0.0151)	0.040(0.0025)*	
GP_AGE05_CAT	β_2	-0.017(0.0005)*	-0.015(0.0054)	-0.010(0.0005)*	-0.006(0.0029)	-0.007(0.0005)*	
AGE05_CAT	β_3	0.035(0.0008)*	0.005(0.0079)	0.037(0.0009)*	0.028(0.0043)*	0.0394(0.0009)*	
GENDER	β_4	-0.044(0.0019)*	0.0001(0.0215)	-0.062(0.0019)*	-0.053(0.0114)*	-0.063(0.0019)*	
FAM_SIZE	β_5	0.141(0.0009)*	0.194 (0.0133)*	0.018 (0.0009)	0.008(0.0059)	0.011(0.0010)*	
PERIOD_D	β_6	-0.017(0.0004)*	-0.011(0.0041)*	0.0003(0.0004)	0.0033(0.0022)	0.001 (0.0004)**	
MAJOR_COVERAGE_YN	β_7	0.256(0.0020)*	0.273 (0.0226)*	0.127(0.0019)*	0.083(0.0120)*	0.100(0.0020)*	
CHRONZ_ATTEST	β_8	0.566(0.0024)*	0.478(0.0257)*	0.184(0.0024)*	0.141(0.0146)*	0.164(0.0024)*	
CHRONZ_FF	β_9	0.266(0.0023)*	0.243(0.0285)*	0.048(0.0023)*	0.060(0.0140)**	0.061(0.0023)*	
MAF	β_{10}	0.307(0.0021)*	0.249 (0.0227)*	-0.029 (0.0020)*	-0.057(0.0125)*	-0.034(0.0020)*	
PF	β_{11}	0.552(0.0022)*	0.943(0.0299)	0.004 (0.0022)	0.041(0.0130)	-0.005(0.0022)*	
KANKER	β_{12}	-0.354(0.0027)*	-0.233 (0.0283)*	-0.237 (0.0026)*	-0.157(0.0145)*	-0.229(0.0027)*	
DEMENT	β_{13}	-0.028(0.0135)*	-0.066(0.1637)	-0.074 (0.0135)*	-0.062(0.0871)	-0.081(0.0136)	
TIME	β_{14}	0.032 (0.0007)*	0.039(0.0116)*	0.048 (0.0008)*	0.066(0.0056)*	0.048(0.0008)*	
AGE05_CAT*TIME	β_{15}	0.004(0.0000)*	0.006(0.0007)*	0.002(0.00005)*	0.003(0.0003)*	0.002(0.00005)*	
DEVIANCE	**G**	31.30	0.63				
DISPERSION	k^{-1}		10.317(0.0712)*		0.8703(0.0089)*		
Inf_Intercept	γ_o			2.702 (0.0958)*	2.688 (0.1840)*	2.701 (0.0958)*	
Inf_GMD	γ_1			0.042(0.0191)*	0.060 (0.0209)	0.039 (0.0191)	
Inf_GP_AGE05_CAT	γ_2			0.011(0.0039)*	0.005(0.0040)	0.0113(0.0039)	
Inf_AGE05_CAT	γ_3			-0.043(0.0036)*	-0.047(0.0038)*	-0.043(0.0036)*	
Inf_GENDER	γ_4			-0.048 (0.0156)*	-0.040 (0.0163)	-0.049(0.0156)*	
Inf_FAM_SIZE	γ_5			-0.233(0.0083)*	-0.217 (0.0088)*	-0.233 (0.0083)*	
Inf_PERIOD_D	γ_6			0.018(0.0029)*	0.016 (0.0030)*	0.018(0.0029)*	
Inf_MAJOR_COVERAGE_YN	γ_7			-0.201(0.0163)*	-0.122(0.0171)*	-0.201(0.0164)*	
Inf_CHRONZ_ATTEST	γ_8			-0.549(0.0189)*	-0.494(0.0196)*	-0.548(0.0189)*	
Inf_CHRONZ_FF	γ_9			-0.285 (0.0198)*	-0.314 (0.0208)*	-0.286(0.0198)*	
Inf_MAF	γ_{10}			-0.372(0.0166)*	-0.371 (0.0172)*	-0.372 (0.0166)*	
Inf_PF	γ_{11}			-1.467(0.0199)*	-1.491 (0.0213)*	-1.468 (0.0199)*	
Inf_KANKER	γ_{12}			0.158 (0.0203)*	0.120 (0.0213)*	0.159 (0.0203)*	
Inf_DEMENT	γ_{13}			-0.082(0.1141)	0.065 (0.1199)	0.039(0.1162)	
Inf_TIME	γ_{14}			-0.0290 (0.00082)*	-0.025 (0.0008)*	-0.029(0.0008)*	
Var	$\sigma 2$					0.012(0.0085)	
Std Deviation	σ_1				0.095(0.0338)		
Std Deviation	σ_2				0.309(0.1118)		
Alpha	α						
Tau	τ						
-2loglikelihood		3161367.6	386201.5	975383	358952	963619	
AIC		3161398.80	386235.51	975445	359020	963683	

** = Border line significance

APPENDIX D

Average Predicted Count Probability



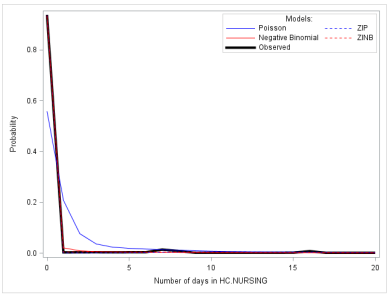
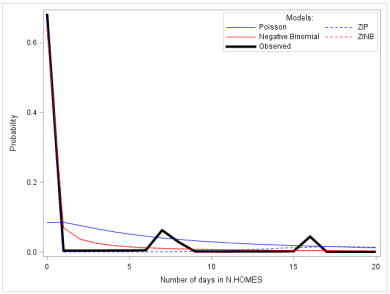


Figure 19: Average Predicted Count Probability



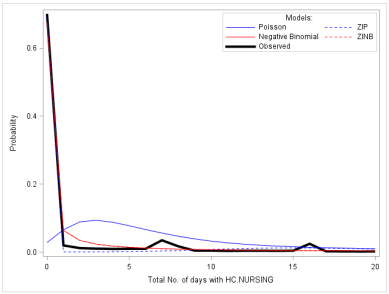
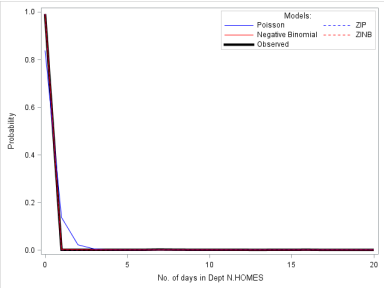


Figure 20: Average Predicted Count Probability



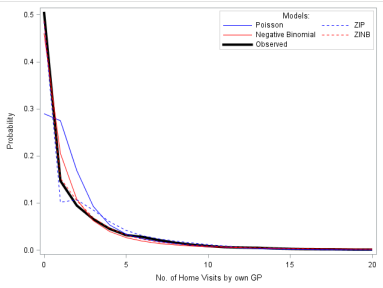


Figure 21: Average Predicted Count Probability

7 APPENDIX E

Table 12: Poisson Model without CC

Effect	Estimate	Standard Error	P-value
Intercept	1.6884	0.06335	0.0001
GMD	-0.0494	0.00342	< .0001
GP_AGE05_CAT	0.007978	0.00109	< .0001
AGE05_CAT	-0.03608	0.00094	< .0001
GENDER	0.05337	0.00428	< .0001
FAM_SIZE	-0.03589	0.00157	< .0001
PERIOD_D	-0.03686	0.00052	< .0001
MAJOR_COVERAGE_YN	0.09392	0.00288	< .0001
CHRONZ_ATTEST	0.2408	0.00358	< .0001
CHRONZ_FF	0.2776	0.00347	< .0001
MAF	0.8753	0.00335	96513 < .0001
PF	-0.1862	0.00382	< .0001
KANKER	0.02226	0.00343	< .0001
DEMENT	0.06306	0.01991	0.0015
TIME	0.04853	0.00122	< .0001
AGE05_CAT*TIME	-0.00034	5.7E-05	¡.0001
GP_AGE05_CAT*TIME	-0.00016	6.8E-05	0.018
GENDER*TIME	-0.00288	0.00027	¡.0001
-2loglikehood			
AIC			

Table 13: Poisson Model with CC

Effect	**Estimate**	**Standard Error**	**P-value**
Intercept	1.6884	0.06335	0.0001
GMD	-0.0494	0.00342	$< .0001$
GP_AGE05_CAT	0.007978	0.00109	$< .0001$
AGE05_CAT	-0.03608	0.00094	$< .0001$
GENDER	0.05337	0.00428	$< .0001$
FAM_SIZE	-0.03589	0.00157	$< .0001$
PERIOD_D	-0.03686	0.00052	$< .0001$
MAJOR_COVERAGE_YN	0.09392	0.00288	$< .0001$
CHRONZ_ATTEST	0.2408	0.00358	$< .0001$
CHRONZ_FF	0.2776	0.00347	$< .0001$
MAF	0.8753	0.00335	$< .0001$
PF	-0.1862	0.00382	$< .0001$
KANKER	0.02226	0.00343	$< .0001$
DEMENT	0.06306	0.01991	0.0015
TIME	0.04853	0.00122	$< .0001$
AGE05_CAT*TIME	-0.00034	5.7E-05	$< .0001$
GP_AGE05_CAT*TIME	-0.00016	6.8E-05	0.018
GENDER*TIME	-0.00288	0.00027	$< .0001$
-2loglikelihood			
AIC			

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Datum: **3/09/2015**