Estimating the relationship between chronic disease progression and costs of care

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1 Introduction

While the ideal platform for economic evaluation of health care interventions designed to delay the progression of chronic disease consists of the continuous monitoring of lifetime costs and effectiveness measures for both treatment and control groups, this is rarely attained. It is far more common to observe data in which intermediate outcome measures are monitored over a relatively short period of time corresponding to a trial or survey horizon. In such circumstances the relationship between intermediate and final outcomes must be modelled using extraneous data. However, data sources which are sufficiently rich to allow these relationships to be estimated rigorously and with statistical significance are not easy to find.

This study is based on an uncensored data set obtained from a retrospective analysis of a prospective study of patients with Alzheimer's Disease. The study explores different ways of estimating the relationship between disease progression and costs of care: survival analysis and panel data methods.

a) survival analysis: regression-based analysis of time to resource event (e.g. time to institutionalisation), with disease progression (measured by cognitive function, behavioural scores and/or activities of daily living) as time dependent covariate, and controlling for age and time from diagnosis.

b) panel data methods: panel data regression analysis of total resource cost per period, as function of disease progression over time, and controlling for time effects, age and individual effects (ie fixed effects model). The paper will also explore whether a random effects model is more suitable.

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2 Background

The results of the study will be relevant to the economic modelling of other chronic disease processes and interventions. Alzheimer's Disease is similar to other disease areas, where therapeutic agents may affect specific markers of disease progression, but where the association between these and other markers of disease progression and treatment costs is inadequately understood. For example, Gilmer et al (1997) examined the hypothesis that glycaemic control in patients with type 2 diabetes, as measured by HbA1c levels, was related to medical care charges for adults with diabetes enrolled in a health maintenance organization (HMO). However, they used cross-sectional data over a 4-year period, which may not accurately represent the association between disease progression and costs over time for individual patients.

A number of estimates of the costs of caring for dementia in England have been made (Gray and Fenn 1993, Souetre 1995, Bosanquet 1999), but these have been based on prevalence data and relatively unsophisticated averaging. Little is known of the longitudinal costs of dementia, for individuals or groups of patients. These costs depend on two important factors, a) the setting in which care is given and b) the progression of dementia, including a range of cognitive and behavioural problems. One published study (Ernst et al 1997) has examined the relationship between cognitive function and patient costs, but this was based on cross-sectional data over a 6-month period only; did not consider behavioural or daily living aspects of disease progression; had a sample size of only 64; and used Californian data with limited generalisability to the UK.

3 Data

3.1 Setting and participants

The data for this study were collected retrospectively from the case notes of 100 subjects (51% male) with a clinical diagnosis of Alzheimer's disease (AD) or vascular dementia recruited to a prospective longitudinal study of behaviour in dementia (Hope et al 1997a, Hope et al 1997b). They were recruited to the study through local general practitioners, community psychiatric nurses and consultant geriatricians. At the start of the study, the subjects were all living at home with a carer who was able to give detailed information about the subject. All subjects lived in Oxfordshire, UK. At 4-monthly intervals the carers were interviewed and the subjects were assessed in terms of their cognition, behaviour, activities of daily living and all health, social and long term care services used. Additional information on the carer's attitude to caring and physical ability to cope was collected at the beginning of the study. The date of the first interviews ranged from

February 1988 to May 1989. The maximum number of interviews was 33 with the final interview for the final subject taking place in August 1999 (see Figure 1).

Out of the 100 patients interviewed at study entry 6 withdrew from the study, and only 1 patient was still alive at August 1999. The mean age at study entry was 78 years (s.d. 6.99), although given the entry criteria all subjects had already been diagnosed with Alzheimer's disease, mean age at diagnosis was 73 years (s.d. 7.50)

3.2 Resource use

A coding frame was designed and information on resource utilisation was extracted from each patient's 4-monthly assessment records on the following: Number and duration of; acute hospitalisations, respite care, outpatient visits, day care, home attendances by district nurses, community psychiatric nurses, home helps or other care assistants, visits by or to the general practitioner or practice nurse. Details on the use of special aids and adaptations such as wheel chairs, bath/bed hoists, incontinence pads and sheets and any special dietary requirements were also recorded. An important aspect of care for a patient with Alzheimer's disease is where the care took place. At each interview it was noted whether the subject still resided at home or had been institutionalized. The point at which subjects were rated as being 'institutionalized' was taken as the time when they were admitted to a hospital ward or a nursing home for permanent care (Hope et al 1998).

3.3 Unit costs

Unit costs were attached to these cost generating events (see Table 1), enabling an estimation of patient specific costs of Alzheimer's disease by 4-month period from study entry to death or censor point. All unit costs were updated to 1998 prices and are reported in UK £ sterling.

3.4 Indicators of disease progression

As part of the original cohort study data was collected every 4 months on the cognitive, behavioural and functional abilities of the patients using the Modified Mini-mental State Examination (MMSE) (Folstein et al. 1995) and the Present Behavioural Examination (PBE) (Hope et al. 1992). The MMSE score ranges from 0 to 30, with a score of zero indicating severe cognitive function. The behavioural and functional data collected using the PBE questionnaire were transcribed on to the Barthel index of activities of daily living. This index measures functional capabilities such as bowel and bladder continence, toilet use, bathing, feeding, grooming, dressing, mobility and ability to cope with stairs. The score ranges from 0 to 20, again with zero indicating the poorest outcome.

3.5 Costs

The average total cost over the 33 interview periods (approximately 11 years) amounts to £ 66,697 (s.d. 60,249). Long stay nursing home, residential home and hospitalisations represent a major component of the total cost (69% of total costs). See figures 2 and 3.

4 Methodology

Given data on the cognitive, functional and behavioural capabilities of patients as their condition progresses, we need to explore ways of establishing the relationship between these measures of progression and the costs incurred caring for the patients. Because the measures of progression change over time and between individuals, and care costs arise as a consequence of discrete resource-generating events, two alternative approaches suggest themselves. First, we could attempt to use time to event data, and relate these to disease progression methods by means of survival analysis techniques with time varying covariates. The limitation of this approach stems from the fact that there are many different events that have resource consequences, and therefore some selection is needed. Alternatively, each of the resource generating events could be assigned a unit cost from reliable sources, and the aggregate of these for each observation interval could be analysed by means of panel data estimation methods, with covariates including the measures of disease progression. A list of variables used in the analyses and their descriptions are displayed in Table 2.

4.1 Survival analysis

Modelling the impact of disease progression on specific events such as admission to residential care requires that the hazard of admission is defined as a function of observed characteristics of the patient as they vary across patients and over time. Death before admission is treated as a censoring event.

We initially rely on a fully parametric specification for the hazard of admission. For example, assuming a conventional loglinear form for the effect of covariates, the empirical Weibull hazard function can be written as:

$$\lambda(t) = \alpha[e^{\beta' x(t)}]t^{\alpha-1} \tag{1}$$

where the covariates x are as defined as above, β is a vector of associated parameters, and t is elapsed time since the condition was diagnosed. The Weibull parameter α determines the time dependence of the baseline hazard: the latter increases or decreases monotonically according to whether $\alpha > 1$

or $\alpha < 1$.[1]By explicitly writing the covariates as a function of time, we allow for the possibility that the covariates will vary as the disease progresses.

The parameters β and α can be estimated through maximisation of the following log likelihood function:

$$L = \sum_{i=1}^{N} [\ln \alpha \left[e^{\beta' x(t)}] t_i^{\alpha-1} - \int_0^{t_i} \alpha [e^{\beta' x(\tau)}] \tau^{\alpha-1} \delta\tau \right] \tag{2}$$

Other distributions conventionally assumed for the hazard function over time, such as the Exponential and the Gompertz, may also be estimated by similar means, and the goodness of fit compared.

We could alternatively estimate a specification for the hazard function which does not imply any particular functional form for the admission hazard over time. A partial likelihood approach suggested by Cox (1972) can be used to estimate a proportional hazard model in which the admission hazard is separated into an unspecified baseline hazard and a conventional loglinear function of the covariates:

$$\lambda(t) = \lambda_0(t)[e^{\beta' x(t)}] \tag{3}$$

where the covariates x are as defined above, β is a vector of associated parameters, and t is elapsed time since the condition was diagnosed. By explicitly writing the covariates as a function of time, we again allow for the possibility that the covariates will vary as the disease progresses. This permits us to test for the impact on time to admission of changes in measured disease progression over time.

Given the proportionality assumption, and a ranking of observed admission times defined as $t_1, ..., t_N$, then the conditional probability that the i'th patient is admitted at t_i, given that any of the patients still at home could have been admitted at t_i, is

$$\frac{e^{\beta' x(t_i)}}{\sum_{j=i}^{N} e^{\beta' x(tj)}} \tag{4}$$

This is the contribution to the likelihood from the i'th observation on time to admission. The product of the individual contributions forms a partial likelihood function which can be estimated by standard techniques. Clearly, only the rank order of admission times is utilised in this procedure, because the baseline hazard $\lambda_0(t)$ cancels out of the ratios. This means that there is no need to specify a functional form for $\lambda_0(t)$, and inferences about the β parameters can be made without any constraints of this kind.

[1]If $\alpha = 1$ the hazard is a simple exponential which is constant over time.

4.2 Panel data analysis

While survival analytic approaches yields benefits in terms of identifying the way that key shifts in the care regime are driven by the rate of disease progression, they do not help determine whether the rate at which costs are accumulated differs within distinct care regimes. To establish the latter, it is necessary to explore variations in the measured aggregate cost per time period for each patient in the sample, and across care regimes. Panel data methods can be utilised in order to estimate the relationships between measured aggregate costs per period and measured disease progression per period within each care regime, controlling for age and gender.

Initially, fixed and random effect models were estimated, and the full results for each are reported in the following section. In principle, the choice between fixed and random effect models depends on whether or not the inferences to be drawn are conditioned on the effects in the sample (Mundlak, 1978; Hsiao, 1985; 1986). In addition however, Hausman's (1978) specification test can be used to determine whether the individual effects are uncorrelated with the other regressors. If this is not the case, the estimators in a random effects model may suffer from inconsistency due to any omitted variables (Greene, 1999, ch. 16). Second, a Lagrange multiplier test due to Breusch and Pagan (1980) uses the OLS residuals to test a model in which random group effects are present against one in which they are not.

5 Results

5.1 Time to permanent institutional care

The conditional probability that a patient diagnosed with Alzheimer's Disease is admitted to long stay care is likely to depend on her physical and mental condition combined with the support available from carers and community services. Tables 3 to 6 show the results for a variety of regressions in which time to admission is used to determine the way these factors affect the hazard of admission. In all regressions a proportional hazard specification is used together with a loglinear form for the impact of covariates (including time-varying covariates). As explained above, the difference between each regression lies in the constraints placed on the functional form for the impact of time itself on the hazard. In the Cox regression, the functional form is determined flexibly, whereas in the Weibull, Exponential and Gompertz regressions, the functional form is determined by the distribution assumed. An appropriate test for the comparative goodness of fit of these functional forms is by reference to the cumulative Cox-Snell residuals (the residuals summed over time periods for each patient). These are graphed against the log of the sample survivor function as a visual test of the model specification. Because the integrated hazard function is known to have an extreme value

distribution with mean 1, the plot should, for a correctly specified model, show a straight line with a 45 degree slope. Figures 4a to 4d show the results of this test for each of the four survival analyses. From inspection, it appears that the best fit arises with the most flexible specification, the Cox regression, with the Weibull form seeming to be the best of the parametric specifications.

The parameter estimates are reported in Tables 3 to 6. They are broadly consistent across the differing functional forms for the hazard, and we discuss the results for each covariate in turn.

5.2 Age and gender

The analysis shows a significant association between age and time to institutionalisation: as age increases, time to institutionalisation falls, indicating an increasing hazard. As all subjects were living at home at entry to the study and had a mean age of 78, this result may have been anticipated; however, it should be noted that this age effect is identified having controlled for disease progression, and is present in all regressions. In contrast, none of the regressions identified a significant association between gender and time to institutionalisation.

5.3 MMSE and Barthel

As noted earlier, an advantage of this study compared to many others in the area is the presence of more than one measure of disease progression, allowing the opportunity to assess the relative importance of cognitive decline and behavioural change/activities of daily living. The results indicate that both the Modified Mini-mental State Examination score and the Barthel index are positively associated with time to institutionalisation: as each declines, duration to institutionalisation also declines. This finding that cognition and behaviour/physical functioning have independent and highly significant ($p < 0.001$ in the Cox regression) in the Cox regression) effects on the likelihood of being institutionalised may have important implications for future study designs and analyses.

5.4 Domestic circumstances

Three of the measures of domestic circumstances available within the study concerned who the subject lived with, the attitude of the carer to caring at baseline, and the physical ability of the carer to cope with caring. The results indicate, firstly, that whereas living with a spouse only does not significantly affect the time to institutionalisation, living with a spouse and others or with family excluding a spouse does seem to significantly increase time to institutionalisation. One possible explanation for this finding is that these carer measures are proxies for carer age: spouses will generally be of

similar age to the subject, whereas other family members are likely to be daughters or sons with more capacity to cope.

The results also indicate that the presence of a carer who has an active preference for caring for the subject at home (as assessed at baseline) significantly increases time to institutionalisation.

Finally, there is no evidence of an independent association between the assessed physical ability of the carer to cope and time to institutionalisation. This may be because attitude is more important than physical ability to care; in addition, some aspects of this measure may already be captured in the variable describing who the subject lives with.

5.5 Costs per period

The results from the panel data analyses on aggregated costs per period are reported in Tables 7 and 8. The model is specified such that each covariate is interacted with a dummy variable indicating whether the patient was in long term residential care (inst=1) or not (inst=0). Table 7 shows the random effects model, and the Breusch Pagan test confirms that there is sufficient heterogeneity in the sample, which needs to be modelled in some way. Table 8 shows the alternative fixed effects specification of the same model, and the Hausman specification test suggests that this is the more appropriate way to model the heterogeneity. The results can again be discussed for each covariate in turn.

5.6 Institutionalisation

As predicted, subjects incur additional costs of approximately £8,000 per 4-month when in an institution, all else held constant. This marginal effect is approximately equivalent to the annual cost of institutional care, as noted in Table 1.

5.7 Age

The fixed effects model indicates that age and the age-institutionalised interaction term are significant but inversely associated with cost. All else held constant, each additional year of age reduces costs incurred per 4-month period by £ 166, while each additional year of age when in an institution has the additional effect of reducing 4-monthly costs by a further £ 159.

These results must be interpreted alongside those related to measures of disease progression (see below). They imply that, having controlled for disease progression, older subjects at home or in institutions are less likely to have health and social care resources committed to them, which may in turn be interpreted as a manifestation of age-related rationing.

5.8 MMSE and Barthel

The results indicate that changes in both MMSE score and Barthel index have an independent and significant effect on costs, but that changes in the Barthel index have a larger impact: each one-point decline in the MMSE score is associated with a £52 increase in costs per 4-month period, whereas each one-point fall in the Barthel index is associated with a £535 increase in costs. Even allowing for the shorter range of the Barthel scale (20 points versus 30 in the MMSE score), it seems from these results that deteriorations in physical or behavioural functioning have a much greater impact than do cognitive changes on the health and social care resources required by people with Alzheimer's Disease.

However, looking at the MMSE/Barthel and institutionalisation interaction terms, it appears that the pattern described above holds only outside institutional care: the coefficients on the cognition and physical/behavioural functioning variables in institutional care effectively cancel those outside institutional care, so that the combined effect is cost-neutral.

6 Conclusion

This study has used a retrospective re-analysis of a prospective long-term cohort study of people with Alzheimer's Disease to explore a series of factors influencing time to institutionalisation and costs of care. An important feature of the original dataset was the presence of frequent and accurate longitudinal assessment of disease progression, and fortuitously a large amount of data on resource use that could be extracted from the study records. In combination, this information has proved particularly valuable, and illustrates that panel data sets - even with relatively small numbers of subjects - are rich sources of information for economists.

The results confirm that previous research has been right to identify the event of institutionalisation as fundamentally important. As Figure 2 showed, the costs incurred in residential or nursing home care or in long-term hospital care accounted for almost 70% of the total care costs of the patients in this study over the entire observed duration of their Alzheimer's Disease. Less expectedly, Figure 2 also identifies respite care as the next most important resource item, accounting for 15% of all costs. This suggests that more attention should be paid to the collection of information on respite care in prospective studies, and to including the onset of need for respite care as an important event in modelling studies.

In contrast to most previous studies, which have assumed costs to be constant once a person with AD is admitted to institutional care, a feature of this study is that the costs of care in institutions do not consist solely of the flat rate cost per week of the institution, but also include such items as general practitioner consultations, out-patient visits and short-term hospital

stays. A valuable extension to this study would be to explore in more detail variation is the actual nursing, care and other resources used by individuals within an institutional setting. Nevertheless, the finding in this study that age is inversely associated with costs of care both at home and in institutional care is intriguing, as it suggests the possible existence of age-related rationing: controlling for everything else, a person with AD appears less likely to get access to health and social care as their age increases.

An important finding of the study is that it may be inappropriate to model disease progression in Alzheimer's Disease solely on the basis of measures of cognitive change. The Modified Mini-mental State Examination score and the Barthel index were found to be independently significant predictors of time to institutionalisation and costs of care, but changes in the Barthel index seem to be much more important than changes in the MMSE score in predicting costs outside institutional care. This finding may have wide-ranging implications for other studies in this area: for example, most pivotal trials of therapies for AD have placed strong emphasis on changes in cognition, and almost all the modelling work done to date on the cost-effectiveness of AD interventions uses the impact of therapy on cognition as the linking mechanism to costs of care.

Finally, and following on from the above point, the empirical estimates of the effects of disease progression on care costs that this study has established should be valuable both in assessing more accurately the true lifetime costs of Alzheimer's Disease and their association with disease progression, and in future work modelling the cost-effectiveness of therapeutic interventions.

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Table 1. Unit costs

Type of good/service		Unit of good service	Source	1998 prices
Hospital admissions[1]	general surgery	per inpatient stay	TFR2 returns	£ 225.77-285.78
	general medicine	per inpatient stay	TFR2 returns	£ 125.09-256.28
	geriatrics	per inpatient stay	TFR2 returns	£ 120.01-157.64
	Psychiatric	per inpatient stay	TFR2 returns	£ 463.75
Outpatient visit[1]		per outpatient visit	TFR2 returns	£ 81.36-110.85
Psychiatrist	Domiciliary visit	per hr of patient contact	Netten, Dennet, Knight (1999)	£ 238.00
GP	Surgery visit	per visit (8.4 mins)	Netten, Dennet (1998)	£ 14.00
	Domiciliary visit	per visit (13.2 mins +12 mins travel)	Netten, Dennet (1998)	£ 46.00
	domiciliary visit-emergency call	per visit (13.2 mins +12 mins travel)	Netten, Dennet (1998)	£ 47.00
	GP telephone	10.8 mins	Netten, Dennet, Knight (1998)	£ 17.00
Practice nurse	Surgery visit	per consultation	Netten, Dennet, Knight (1998)	£ 7.29
Respite care	Community hospital	per inpatient day	TFR2 returns	£ 125.09
	Teaching hospital wards	per inpatient day		See above
	Private nursing home	per inpatient day (based on care package of short term resident week)	Netten, Dennet, Knight (1999)	£ 55.70
Day care		per hour	Netten, Dennet, Knight (1999)	£ 4.75
Domiciliary help	District nurse	per domiciliary visit	Netten & Dennett (1998)	£ 15.00
	Chiropodist	per domiciliary visit	Netten, Dennet, Knight (1999)	£ 15.00
	Care assistant	per domiciliary visit (2 hr session)	CIPFA	£ 25.00
	CPN	per domiciliary visit	Netten, Dennet, Knight (1998)	£ 20.00
	Other helper eg OT, physio	per domiciliary visit	Netten, Dennet, Knight (1998)	£ 35.00

Aids and adaptations	Wheel chair, walking frame, Hoist	per day	Netten, Dennet, Knight (1998)	£	0.40
	Incontinence pads	per pad	Personal communication	£	0.01
	Kylie/inco sheets	per sheet	Personal communication	£	0.05
	Enema	per enema	Personal communication	£	3.00
Accommodation	Residential home[2]	per day	Personal communication (4 homes)	£	31.42-61.43
	Nursing home[2]	per day	Personal communication (9 nursing homes)	£	54.42-82.14

[1] Based on six Oxfordshire based hospitals; hospital specific costs were attached to the hospital specific resource use information

2 Based on a survey of residential and nursing homes used by subjects in the study. Where homes failed to respond, unit costs are taken to be the average of the responders.

Table 2. Description of variables used in the analyses

Variable	Description	Frequency (n=1094)	Mean	SD
Inst	Institutionalised = 1	388		
	Not Institutionalised = 0	698		
age_1	Patient age	1092	79	6.58
mmse	MMSE score ranges from 0-30	966	8.71	8.79
barthel	Barthel score ranges from 0-20	982	12.25	6.35
Igende_0	Gender = male	495		
Igende_1	Gender = female	599		
Ilivin_0	Living alone	47		
Ilivin_1	Living with spouse	699		
Ilivin_2	Living with spouse & others	74		
Ilivin_3	Living with family (excluding spouse)	214		
Ilivin_4	Living with others (non family)	58		
Impbe1_1	Resents having to care for patient	60		
Impbe1_2	Caring because they feel they ought to	70		
Impbe1_3	No resentment to caring	964		
Impela1	Not coping with caring	0		
Impela2	Is coping but only just	124		
Impela3	Moderately fit and able to do all that is necessary	289		
Impela4	Physically fit and able to cope easily	681		

Table 3: Cox regression on time to institutionalisation

```
No. of subjects =          100                     Number of obs   =       100
No. of failures =           69
Time at risk    =  69.00000003
                                                    LR chi2(12)     =     54.75
Log likelihood  =   -223.18015                      Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t |
          _d |      Coef.   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
       age_1 |  -.0619412   .0246643     -2.511   0.012      -.1102823   -.0136001
        mmse |   .1045333   .0298725      3.499   0.000       .0459843    .1630823
     barthel |    .135476   .0353711      3.830   0.000       .0661499    .2048021
    Igende_1 |   .2748704   .3129597      0.878   0.380      -.3385193    .8882601
    Ilivin_1 |   .4998674   .5842072      0.856   0.392      -.6451576    1.644892
    Ilivin_2 |    1.97022   .7728395      2.549   0.011       .4554826    3.484958
    Ilivin_3 |   1.150655   .6056404      1.900   0.057      -.0363781    2.337689
    Ilivin_4 |   .9231766   .7451839      1.239   0.215       -.537357     2.38371
    Impbe1_2 |  -.5268318    .717165     -0.735   0.463      -1.932449    .8787858
    Impbe1_3 |   1.466168   .6346033      2.310   0.021       .2223679    2.709967
    Impbe1a3 |   -.615468   .4410316     -1.396   0.163      -1.479874     .248938
    Impbe1a4 |  -.2355714   .4028463     -0.585   0.559      -1.025136    .5539929
------------------------------------------------------------------------------
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Table 4: Weibull regression on time to institutionalisation

```
No. of subjects =          100                     Number of obs   =       100
No. of failures =           69
Time at risk    =  69.00000003
                                                    LR chi2(12)     =     59.88
Log likelihood  =   -102.47644                      Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t |      Coef.   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
       age_1 |  -.0573205    .024983     -2.294   0.022      -.1062862   -.0083548
        mmse |   .0923961   .0292013      3.164   0.002       .0351626    .1496295
     barthel |   .1571005   .0357637      4.393   0.000       .0870049    .2271961
    Igende_1 |   .4054618   .3061179      1.325   0.185      -.1945182    1.005442
    Ilivin_1 |   .7340117   .5718376      1.284   0.199      -.3867695    1.854793
    Ilivin_2 |   2.166675   .7527565      2.878   0.004       .6912993    3.642051
    Ilivin_3 |   1.239739   .6109803      2.029   0.042       .0422401    2.437239
    Ilivin_4 |   1.050225   .7341347      1.431   0.153      -.3886528    2.489102
    Impbe1_2 |  -.2949762   .7094583     -0.416   0.678      -1.685489    1.095536
    Impbe1_3 |   1.372174   .6332658      2.167   0.030       .1309957    2.613352
    Impbe1a3 |  -.6853665   .4373387     -1.567   0.117      -1.542535    .1718017
    Impbe1a4 |  -.3473264   .4042383     -0.859   0.390      -1.139619    .4449662
       _cons |   1.112882     2.2664      0.491   0.623       -3.32918    5.554944
-------------+----------------------------------------------------------------
       /ln_p |   .4135745   .0919579      4.497   0.000       .2333404    .5938086
-------------+----------------------------------------------------------------
           p |   1.512214   .1390599                          1.262811    1.810872
         1/p |   .6612823   .0608101                          .5522201     .791884
------------------------------------------------------------------------------
```

Table 5: Exponential regression on time to institutionalisation

```
No. of subjects =          100                     Number of obs   =       100
No. of failures =           69
Time at risk    =  69.00000003
                                                   LR chi2(12)     =     43.93
Log likelihood  =   -110.74931                     Prob > chi2     =    0.0000

------------------------------------------------------------------------------
          _t |      Coef.   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
       age_1 |  -.0388429   .0233812     -1.661   0.097      -.0846691    .0069834
        mmse |   .0543368   .0262198      2.072   0.038       .002947    .1057267
     barthel |   .1011396    .031738      3.187   0.001       .0389342     .163345
    Igende_1 |   .2664258   .2930767      0.909   0.363      -.3079941    .8408457
    Ilivin_1 |   .3600802   .5534297      0.651   0.515       -.724622    1.444782
    Ilivin_2 |   1.241129    .710527      1.747   0.081      -.1514784    2.633736
    Ilivin_3 |   .7976743   .5708475      1.397   0.162      -.3211662    1.916515
    Ilivin_4 |   .4491843    .708473      0.634   0.526      -.9393972    1.837766
    Impbe1_2 |  -.0909598   .6935728     -0.131   0.896      -1.450337    1.268418
    Impbe1_3 |   .9216973   .6096013      1.512   0.131      -.2730992    2.116494
    Impbe1a3 |  -.3901907   .4226214     -0.923   0.356      -1.218513    .4381319
    Impbe1a4 |  -.1780716   .3926093     -0.454   0.650      -.9475716    .5914284
       _cons |   .9093234   2.180145      0.417   0.677      -3.363681    5.182328
------------------------------------------------------------------------------
```

Table 6: Gompertz regression on time to institutionalisation

```
No. of subjects =          100                     Number of obs   =       100
No. of failures =           69
Time at risk    =  69.00000003
                                                   LR chi2(12)     =     39.95
Log likelihood  =   -110.18608                     Prob > chi2     =    0.0001

------------------------------------------------------------------------------
          _t |      Coef.   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
       age_1 |  -.0421401   .0238363     -1.768   0.077      -.0888583    .0045782
        mmse |   .0583504   .0266846      2.187   0.029       .0060496    .1106512
     barthel |   .1127012   .0337571      3.339   0.001       .0465385    .1788638
    Igende_1 |   .3122482   .2970236      1.051   0.293      -.2699075    .8944038
    Ilivin_1 |   .4510251   .5614589      0.803   0.422      -.6494142    1.551464
    Ilivin_2 |   1.419379   .7301477      1.944   0.052      -.0116841    2.850442
    Ilivin_3 |   .8728482   .5803348      1.504   0.133      -.2645871    2.010283
    Ilivin_4 |   .5858436   .7225929      0.811   0.418      -.8304124      2.0021
    Impbe1_2 |  -.0841096   .6959549     -0.121   0.904      -1.448156    1.279937
    Impbe1_3 |   .9454691   .6134666      1.541   0.123      -.2569033    2.147842
    Impbe1a3 |  -.4286942   .4259001     -1.007   0.314      -1.263443    .4060548
    Impbe1a4 |  -.2250969    .396987     -0.567   0.571      -1.003177    .5529833
       _cons |   .8241318   2.197959      0.375   0.708      -3.483788    5.132051
-------------+----------------------------------------------------------------
       gamma |   .1859009   .1696243      1.096   0.273      -.1465565    .5183584
------------------------------------------------------------------------------
```

Table 7: Random-effects GLS regression

```
                                                Number of obs      =      1092
Group variable (i) : patient                    Number of groups   =       100

R-sq:  within  = 0.2550                         Obs per group: min =         2
       between = 0.2334                                        avg =      10.9
       overall = 0.2422                                        max =        32

Random effects u_i ~ Gaussian                   Wald chi2(7)       =    362.32
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
    tc_1 |      Coef.   Std. Err.       z     P>|z|       [95% Conf. Interval]
---------+--------------------------------------------------------------------
    inst |   7633.243   4015.957      1.901   0.057      -237.8873    15504.37
   age_1 |    17.0957   43.01067      0.397   0.691      -67.20368    101.3951
IiXage_1 |  -147.8541   49.14079     -3.009   0.003      -244.1683   -51.53995
    mmse |  -66.26761   24.72219     -2.680   0.007      -114.7222   -17.81302
IiXmms_1 |   70.10112   37.74036      1.857   0.063      -3.868623    144.0709
 barthel |   -436.682   41.51034    -10.520   0.000      -518.0408   -355.3233
IiXbar_1 |   481.5542   59.30823      8.120   0.000       365.3122    597.7962
   _cons |   10608.44   3564.886      2.976   0.003       3621.388    17595.48
---------+--------------------------------------------------------------------
 sigma_u |  2493.5364
 sigma_e |  3609.8231
     rho |  .32302304   (fraction of variance due to u_i)
------------------------------------------------------------------------------


Breusch and Pagan Lagrangian multiplier test for random effects:

        tc_1[patient,t] = Xb + u[patient] + e[patient,t]

        Estimated results:
                             Var     sd = sqrt(Var)
                    ---------+-----------------------------
                        tc_1 |   2.63e+07       5123.513
                           e |   1.30e+07      3609.8231
                           u |    6217724      2493.5364

        Test:   Var(u) = 0
                                chi2(1) =   521.49
                              Prob>chi2 =     0.0000
```

Table 8: Fixed-effects (within) regression

```
                                                Number of obs      =      1092
Group variable (i) : patient                    Number of groups   =       100

R-sq:  within  = 0.2589                         Obs per group: min =         2
       between = 0.1432                                        avg =      10.9
       overall = 0.1815                                        max =        32

                                                F(7,985)           =     49.15
corr(u_i, Xb)  = -0.2628                        Prob > F           =    0.0000

------------------------------------------------------------------------------
    tc_1 |      Coef.   Std. Err.       t     P>|t|       [95% Conf. Interval]
---------+--------------------------------------------------------------------
    inst |   7958.857    4267.36      1.865   0.062      -415.3054    16333.02
   age_1 |   -166.271   100.4636     -1.655   0.098      -363.4184    30.87627
IiXage_1 |  -159.4127   52.21677     -3.053   0.002      -261.8816    -56.9438
    mmse |  -52.87509   26.68523     -1.981   0.048      -105.2415   -.5086459
IiXmms_1 |   49.70875   38.22206      1.301   0.194      -25.29727    124.7148
 barthel |  -535.4129   49.18883    -10.885   0.000      -631.9399    -438.886
IiXbar_1 |   536.1549   61.42445      8.729   0.000        415.617    656.6927
   _cons |   26295.66   8212.839      3.202   0.001       10178.99    42412.33
------------------------------------------------------------------------------
 sigma_u |  3384.3092
 sigma_e |  3609.8231
     rho |   .4677902   (fraction of variance due to u_i)
------------------------------------------------------------------------------
F test that all u_i=0:     F(99,985) =     6.67              Prob > F = 0.0000
```

Hausman specification test

```
            ---- Coefficients ----
         |      Fixed       Random
    tc_1 |    Effects      Effects       Difference
---------+-----------------------------------------
    inst |   7958.857     7633.243         325.6135
   age_1 |   -166.271      17.0957        -183.3667
IiXage_1 |  -159.4127    -147.8541        -11.55857
    mmse |  -52.87509    -66.26761         13.39253
IiXmms_1 |   49.70875     70.10112        -20.39237
 barthel |  -535.4129     -436.682        -98.73087
IiXbar_1 |   536.1549     481.5542         54.60064

Test:  Ho:  difference in coefficients not systematic

             chi2(  7) = (b-B)'[S^(-1)](b-B), S = (S_fe - S_re)
                       =    32.59
             Prob>chi2 =     0.0000
```

Figure 1. Percentage of subjects available at interview

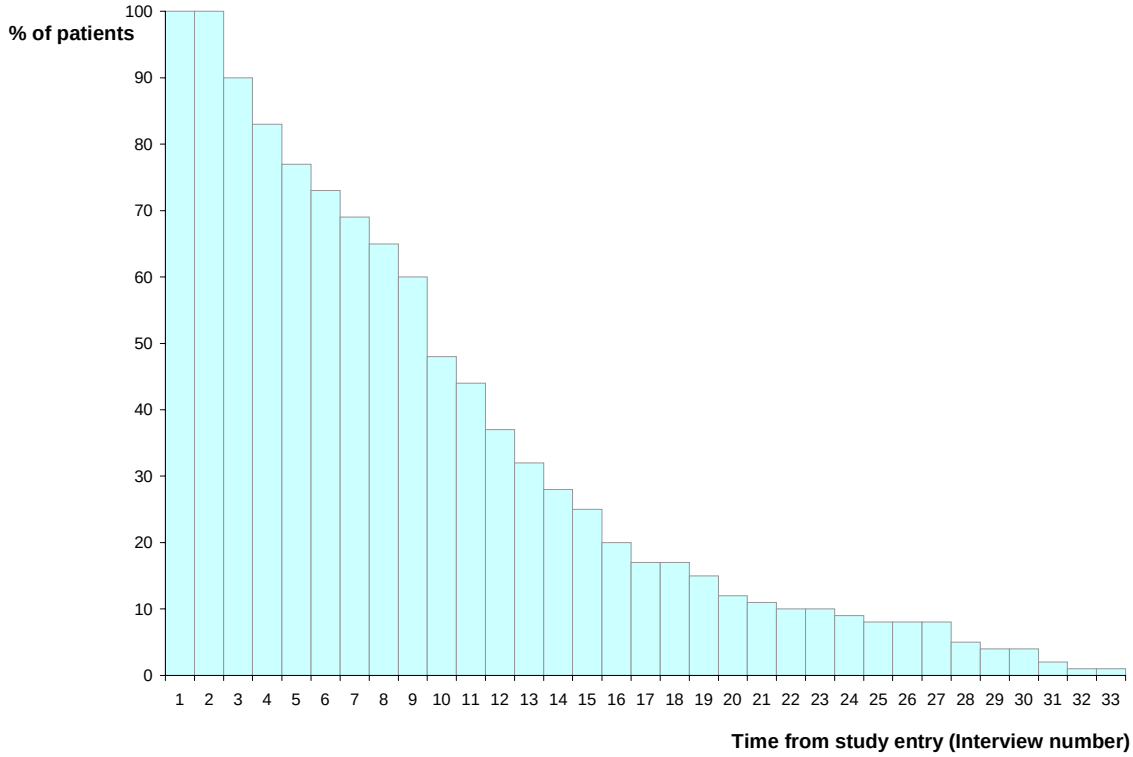

Figure 2. Components of total cost

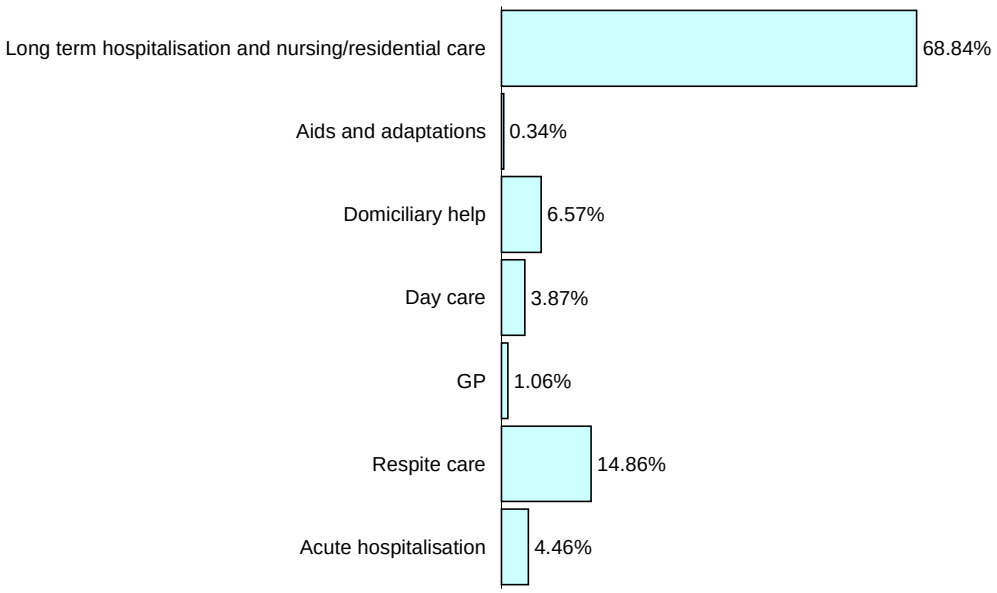

Figure 3. Average cost per 4-month period (interview 1 costs based on 4 weeks prior to study entry)

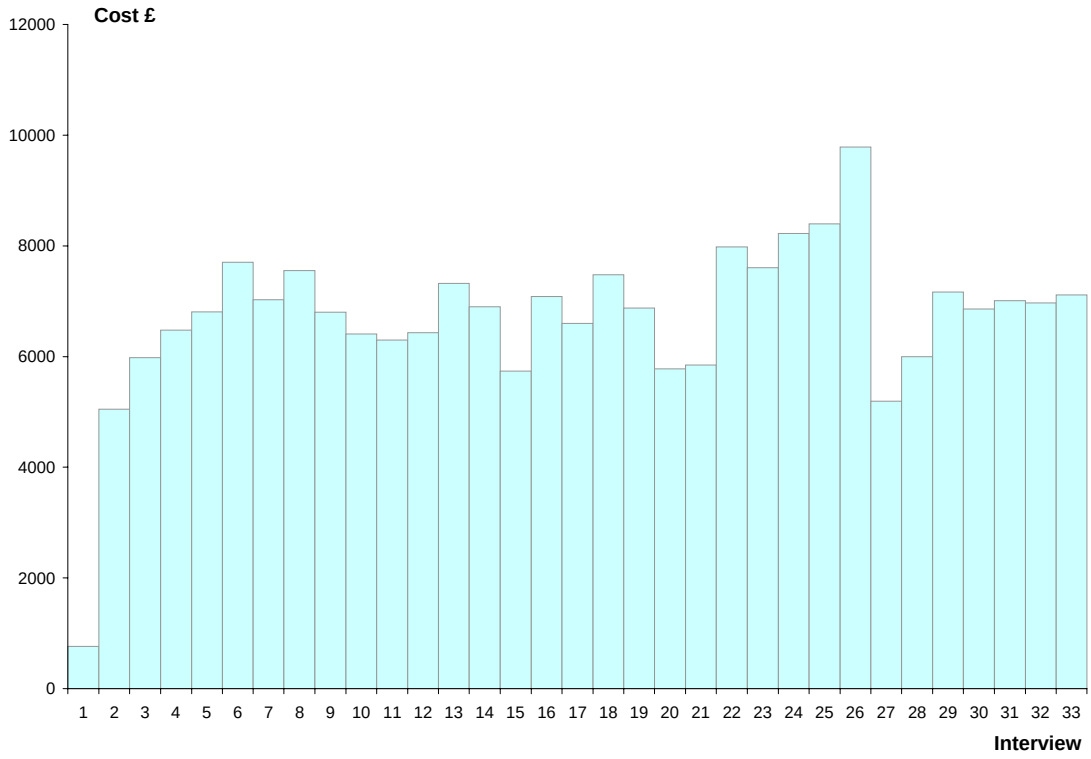

Figure 4a: Cox –Snell residual analysis for Cox regression

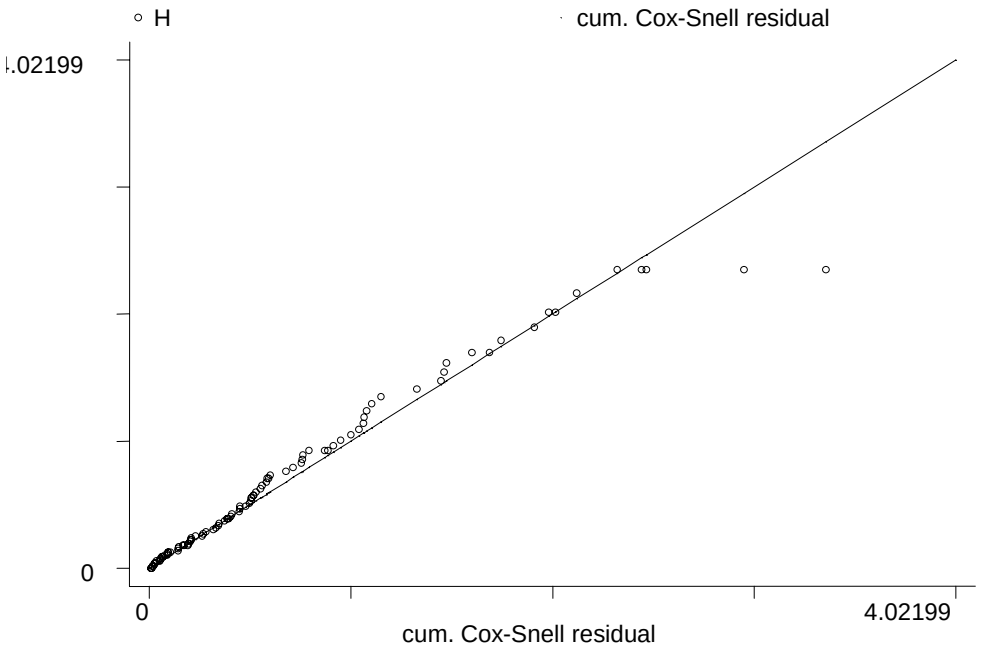

Figure 4b: Cox –Snell residual analysis for Weibull regression

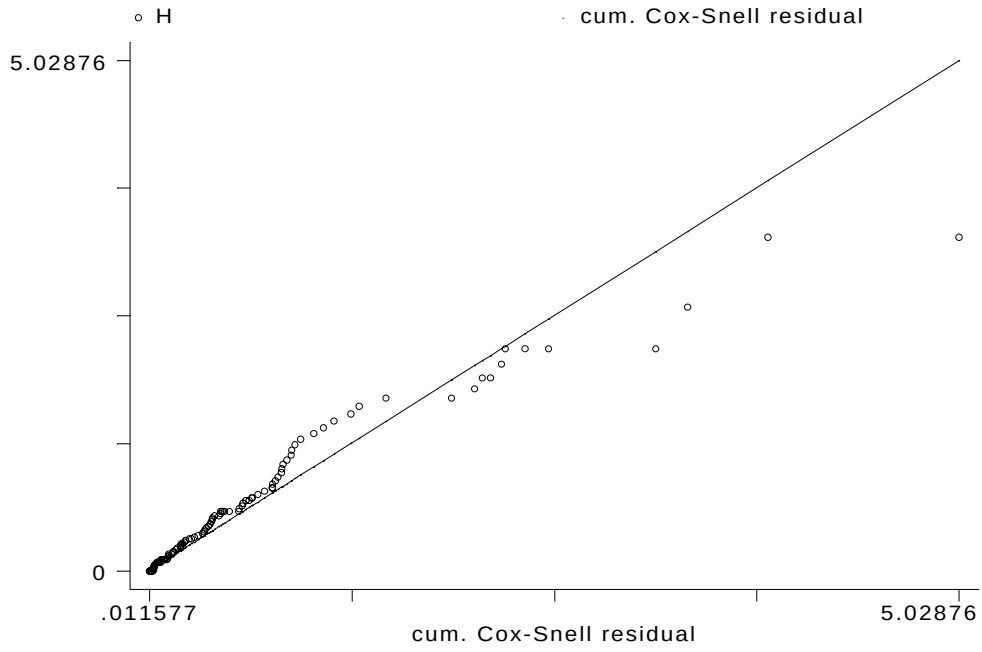

Figure 4c: Cox –Snell residual analysis for Exponential regression

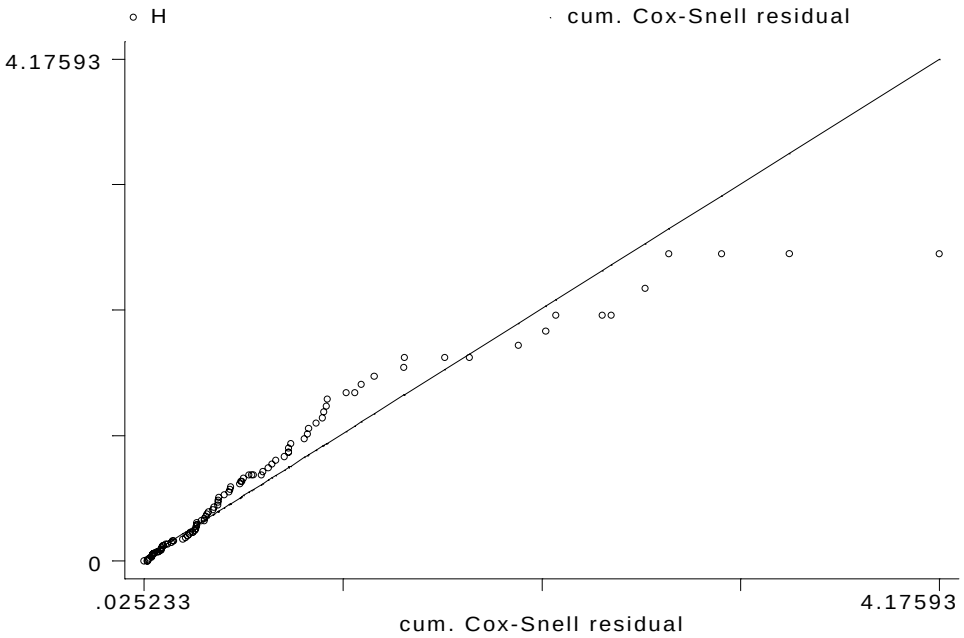

Figure 4d: Cox –Snell residual analysis for Gompertz regression