Policy Research Unit in Economic Evaluation of Health & Care Interventions

Policy Research Unit in Economic Evaluation of Health & Care Interventions (EEPRU)

ESTIMATING INFORMAL CARE EFFECTS ASSOCIATED WITH EQ-5D TARIFF VALUES FOR USE IN ECONOMIC EVALUATION

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Report 012

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EXECUTIVE SUMMARY

This report presents the findings of a study that estimates informal care need using the health of the patient measured by EQ-5D, ICD chapter and other health and sociodemographic data. The results can be used to predict changes in informal care associated with changes in the health of the patient measured using EQ-5D.

Methods

Data was used from a prospective survey of inpatients and contained 59,512 complete responses across 44,494 individuals. The number of days a friend or relative has needed to provide care or help with normal activities in the last six weeks was estimated using the health of the patient measured by EQ-5D, ICD chapter and other health and sociodemographic data. A variety of different regression models were estimated that are appropriate for the distribution of the informal care dependent variable, which had large spikes at 0 (zero informal care) and 42 days (informal care every day).

Results

The preferred model that most accurately predicted the distribution of the data was the zero-inflated negative binomial with variable inflation. The results indicated that improving the health of the patient reduces informal care need. Patients with comorbidities had greater informal care need. The relationship between ICD chapter and informal care need was not as clear.

Discussion

The preferred zero-inflated negative binomial with variable inflation model can be used to predict changes in informal care associated with changes in the health of the patient measured using EQ-5D, and these results can be applied to existing datasets to inform economic evaluation. Limitations included recall bias and response bias of the informal care data, and restrictions of the dataset to exclude some patient groups.

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1 INTRODUCTION

The impact of informal care is taken into account in economic evaluation if a societal perspective is used, where the benefits of an intervention include both the direct health of the patient and wider societal benefits, and costs include those incurred by the health system and those borne by society. This can help avoid an inefficient allocation of resources as the focus is not solely on costs to the publicly funded health system, as it takes into account the full societal effects of an intervention. In the UK the National Institute for Health and Care Excellence (NICE) reference case for health technology assessment does not recommend the routine inclusion of wider societal costs or benefits. The reference case takes the perspective that benefits should be measured by direct health effects using EQ-5D (although this can include carer health), and costs should only include those incurred by the National Health Service (NHS) and personal and social services (PSS).[1] However, from January 2014 Value-Based Pricing (VBP) will be used to assess the value of new medicines, and scoping documents have outlined that a perspective should be taken that recognises the wider societal benefits and costs of interventions.[2] In order to take into account the costs of informal care for an intervention, informal care needs to be first measured and then valued using the appropriate costings for the type of care provided.

Informal care is care provided by friends, family and volunteers to individuals who would have difficulty managing without this care. The informal care economy is substantial, with almost 6 million carers in the UK alone, recorded in the 2001 census.[3] However informal care is difficult to measure and value. In terms of measurement, the issue of joint production is important to recognise and correct in order to avoid inflated estimates.[4] For valuation, it is important to recognise that informal care is a non-market or quasi-market of services supplied by carers who are often unpaid, or who receive only nominal payments or state benefits that do not reflect the true cost or benefits of the care.[5]

Typically informal care is measured using time spent caring, but it is difficult to distinguish informal care activities from usual household activities that would be undertaken regardless. A range of methods have been used to record time spent providing care, such as a time diary, recall,[4, 6] experience sampling and direct observation, each with their own advantages and disadvantages. Time spent providing informal care can then be given a monetary value using a range of techniques: revealed preference using the opportunity cost, proxy good or wellbeing valuation method; or stated preference using discrete choice experiments or contingent valuation.[6-8] The monetary values that are produced by these methods can then be incorporated alongside other costs of an intervention. Informal care can also be valued using non-monetary valuation which captures the effect on the carer who provides the care; for example, by measuring their health-related quality of life using a generic preference-based measure such as EQ-5D,[9] or by measuring their care-related quality of life[10] or carer experience.[11] These utility or quality of life values can then be included alongside other benefits of an intervention. Including the utility of the carer alongside the utility of the patient is straightforward if it is assumed that both should be given an equal weighting, but combining patient utility valued using EQ-5D and carer quality of life using a different measure is less straightforward. The incorporation of costs of informal care into the overall cost of an intervention is more straightforward as they are all measured using the same monetary value. However, it is important to ensure no double-counting, as the same impact from informal care cannot be measured using both costs and benefits. Willingness to accept valuations of carer time, for example, are likely to include an element of compensation for the reduction in health-related quality of life that is anticipated when caring duties are undertaken.

If informal care is to be included as a cost in economic evaluation, then the differences in informal care costs across interventions are required. However many studies that are used to inform economic evaluation have not collected data that includes the direct measurement of informal care time across interventions. One solution is to use data that is typically collected on the health of the patient to predict the informal care required for each intervention. Of interest is how informal care changes as the EQ-5D utility score of the patient changes, given the use of EQ-5D to capture the direct health effects in economic evaluations submitted to NICE. One exploratory study used Ordinary Least Squares (OLS) regression to estimate days of informal care used by EQ-5D utility score.[12] However, there were limitations with this study as it did not model the difference by health condition and did not use models that are most appropriate for the data.

This paper estimates informal care usage associated with the health of the patient, building upon the approach taken by Dixon et al (2006).[12] The analysis is based around the linkage between informal carer time, EQ-5D and ICD chapter. Regressions are estimated that can be used to predict informal care using the EQ-5D and ICD chapter of the patient. This would enable measurement of the impact of health technologies on informal carer time via their impact on patient health. The informal carer time can then be given a monetary value using existing methods in the literature. These results can be applied to existing datasets to inform economic evaluation.

2 METHODS

2.1 Data

The Health Outcomes Data Repository (HODaR) is a dataset collated by Cardiff Research Consortium.[13] The data is collected from a prospective survey of inpatients and outpatients at Cardiff and Vale NHS Hospitals Trust, which is a large University hospital in South Wales, UK. The survey is linked to existing routine hospital health data to provide a dataset with socio-demographic, health-related quality of life and ICD classification data. The survey includes all subjects aged 18 years or older and excludes individuals who are known to have died. The survey also excludes people with a primary diagnosis on admission of a psychological illness or learning disability. This study focuses on the inpatient sample which has 96,282 eligible observations across 66,113 individuals discharged from hospital between April 2002 and January 2009; of these there are 59,512 complete responses across 44,494 individuals for all variables used in the analysis and this is the sample used here.

2.2 Measures

2.2.1.1 Informal care

The informal care data was self-reported by the patient and recorded the number of days a friend or relative had to provide care or help with normal activities in the last six weeks. Raw observations had a maximum of 45 days, though the data was censored at 42 days, the maximum number of days in 6 weeks.

2.2.1.2 Health and socio-demographics

The health of the patient was measured using EQ-5D, a preference-based measure with 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each with 3 levels of severity.[14] The preference weights used here were elicited using time-trade-off with a sample of 2,997 members of the UK general population and modelled to produce a utility value for every health state.[9] ICD chapter dummy variables had a value of 1 where the ICD chapter was recorded in the first ICD classification of the patient during their hospital visit. An operation dummy variable had a value of 1 if the patient had an operation during their hospital visit, and a comorbidities dummy variable had a value of 1 if multiple ICD chapters were recorded during the hospital visit. The age of the patient was measured at the time of the survey.

2.3 Analysis of data

2.3.1.1 Descriptive analysis

Descriptive statistics of the sample were generated. The distribution of EQ-5D and days the patient needed informal care have also been presented.

2.3.1.2 Modelling the data for the econometric models

Regression analysis was used to estimate the relationship between the health of the patient, measured using EQ-5D and ICD chapter, and days of informal care required in the last 6 weeks. Individual patient-level data was used to make the best use of the variability of responses in the available dataset.

Several properties of the data needed to be considered before identifying the most appropriate method for modelling 'days of informal care in the last 6 weeks'. The variable was a count data variable, the distribution was skewed with a very large spike at zero days and another spike at 42 days, and had some repeated observations per patient. The large spike in response at zero days is common in this type of data and reflects the large number of people who did not require informal care after discharge. The spike at 42 days was a consequence of a decision to truncate the distribution of observations, which had a maximum of 45 days. There were also smaller spikes at multiples of 5 and 7 days, usually due to individuals rounding off responses. To reduce the impact of these smaller peaks in the data on the analysis, models are often estimated in the literature grouping the dependent variable. In the analysis reported here these smaller spikes were ignored since grouping the dependent variable would not allow estimation of all parameters of interest. Although some respondents have multiple observations, the majority do not. There were only 10,330 out of 44,494 respondents with multiple responses and these respondents had a median of 2 repeated observations.

Although linear regression models based on continuous variables are often applied to count data variables, this may result in biased, inconsistent and inefficient estimates, therefore this approach is not used here. Alternative models that are appropriate for this type of data were estimated and compared before choosing the preferred model. For completeness, some random effects models were estimated to address the issue that some respondents have multiple observations but given the small number of repeated observations robust standard errors can also be used to take into account clustering. The estimated models used were Tobit; Poisson; random effects Poisson;

negative binomial; two-part model (using probit and truncated negative binomial); zero-inflated negative binomial,[1] and are described below. For the preferred model the exclusion of variables is explored for insignificant variables and variables that may not always be available to inform economic evaluation.

2.3.1.3 Models

A Tobit model is the only one out of all the models estimated here that ignores the count nature of the data. However, it allows for the spikes at both ends of the distribution. The model is specified as:

$$y_i = \mathbf{x}_i'\boldsymbol{\beta} + \varepsilon_i \tag{1a}$$

$$y = \begin{cases} 0 & \text{if } y^* \leq 0 \\ y^* & \text{if } 0 < y^* < 42 \\ 42 & \text{if } y^* \geq 42 \end{cases} \tag{1b}$$

where the dependent variable, y_i, represents days needed informal care for patient i; $\mathbf{x}_i$ is a vector of explanatory variables including EQ-5D score, dummies for ICD chapter, comorbidities and operation as well as socio-demographic characteristics of age, age-squared and female; $\boldsymbol{\beta}$ is the corresponding vector of parameters to be estimated; and ε is the usual independent and identically normally distributed zero mean error term.

The Poisson and negative binomial regression models are related. The Poisson regression model assumes that the observed counts are drawn from a Poisson distribution with a mean μ_i given by:

$$\mu_i = E(y_i \mid \mathbf{x}_i) = \exp(\mathbf{x}_i'\boldsymbol{\beta}) \tag{2}$$

The Poisson distribution rarely fits well in practice because of the well-known and restrictive equidispersion property, that is, the Poisson distribution variance equals its mean. In most applications, the variance usually exceeds the mean, a feature called overdispersion. The negative binomial overcomes this problem by introducing unobserved heterogeneity among observations in the form of an error term, ξ_i, uncorrelated with the independent variables as follows:

[1]The random effects negative binomial model was also considered but was abandoned due to convergence difficulties.

$$\eta_i = \exp\left(\mathbf{x}_i^{'}\boldsymbol{\beta} + \xi_i\right) \tag{3}$$

Assuming that $E[\exp(\xi)] = 1$ the expected conditional mean of the negative binomial regression can be written as:

$$E[\eta_i] = E(y_i \mid \mathbf{x}_i) = \exp\left(\mathbf{x}_i^{'}\boldsymbol{\beta}\right) \tag{4}$$

It is clear from equations (2) and (4) that both the Poisson and the negative binomial regression share the same mean structure. If the assumptions underlying the negative binomial regression are supported by the data the conditional expected rate of counts will be the same for both models but the standard errors of the Poisson regression model will be biased downwards.

Overdispersion can arise not only from unobserved heterogeneity but also from different processes generating the first and subsequent events, that is, more zeroes in the data than can be generated by the Poisson or even the negative binomial regression models. There are two leading modified count models that can be used to deal with this problem: the two-part model and the zero-inflated model.

The two-part or hurdle model relaxes the assumption that the zeroes and positive counts are generated by the same process. It combines a binary model (a probit or a logit) to predict the zeroes with a zero truncated Poisson or negative binomial regression to predict positive counts. In this model, zero is a hurdle to overcome before any positive counts can be attained and it is often interpreted as a two stage decision making process. Using a probit model for the binary outcome and a truncated negative binomial, the two-part model can be defined by the following two equations:

$$\Pr(y_i = 0 \mid \mathbf{z}_i) = \Phi\left(\mathbf{z}_i^{'}\boldsymbol{\gamma}\right) \tag{5a}$$

and

$$\Pr(y_i \mid y_i > 0, \mathbf{x}_i) = \frac{\Pr(y_i \mid \mathbf{x}_i)}{1 - \left(1 + \alpha e^{\mathbf{x}_i^{'}\boldsymbol{\beta}}\right)^{-1/\alpha}} \tag{5b}$$

where $\mathbf{z}_i$ is a vector of random variables which determine the probability of a zero in the data, $\boldsymbol{\gamma}$ is the corresponding parameter vector and $\Pr(y_i \mid \mathbf{x}_i)$ is:

$$\Pr(y_i = m \mid \mathbf{x}_i) = \frac{\Gamma(y_i + \alpha^{-1})}{y_i! \Gamma(\alpha^{-1})} \left(\frac{\alpha^{-1}}{\alpha^{-1} + e^{\mathbf{x}_i' \boldsymbol{\beta}}} \right)^{\alpha^{-1}} \left(\frac{e^{\mathbf{x}_i' \boldsymbol{\beta}}}{\alpha^{-1} + e^{\mathbf{x}_i' \boldsymbol{\beta}}} \right)^{y_i} \tag{6}$$

where $\Gamma(\ )$ is the gamma function and α is the degree of dispersion. The vector $\mathbf{z}_i$ could in principle be identical to $\mathbf{x}_i$.

The zero-inflated model allows the zeroes to be generated by two different processes. It supplements the Poisson or the negative binomial regression with a binary model to increase the zero count. It is often interpreted as heterogeneity in the population arising from two distinct unobserved groups. The outcome for one group (group 1) is zero with probability one. For the other group (group 2) the outcome might be zero but with a positive probability of a nonzero outcome. The zero-inflated negative binomial can be estimated using inflation of only the constant term or inflation of explanatory variables and the constant term. The zero-inflated negative binomial model can be defined by the negative binomial in equation (3) together with a logit model for the probability of group membership:

$$\Pr(\text{group } 1 \mid \mathbf{z}_i) = \frac{e^{\mathbf{z}_i' \boldsymbol{\gamma}}}{1 + e^{\mathbf{z}_i' \boldsymbol{\gamma}}} \tag{7}$$

The predicted probabilities of the counts for the negative binomial model can be computed by substituting the estimated parameter values in equation (6). The expected counts for the model are found using the formula below:

$$E(y_i \mid \mathbf{x}_i, \mathbf{z}_i) = \left(1 - \frac{e^{\mathbf{z}_i' \boldsymbol{\gamma}}}{1 + e^{\mathbf{z}_i' \boldsymbol{\gamma}}} \right) e^{\mathbf{x}_i' \boldsymbol{\beta}} \tag{8}$$

STATA version 11 was used for all regression analysis and IBM SPSS version 19 was used for the descriptive statistical analysis.

3 RESULTS

3.1 Descriptive statistics

Table 1 presents descriptive statistics of the sample. The mean EQ-5D score in the sample was 0.652 (s.d.=0.321) and mean age was 59.00 (s.d.=17.34). Figure 1 shows that the distribution of EQ-5D score was tri-modal and there were observations across the full range of utilities (1 to -0.594). The number of observations in each ICD chapter varied greatly, with larger proportions of patients in ICD chapter I (diseases of the circulatory system), K (diseases of the digestive system), and M (diseases of the musculoskeletal system and connective tissue), and few observations for A and B (infectious and parasitic diseases), F (mental and behavioural disorders), and Q (congenital malformations, deformations and chromosomal abnormalities). There were no observations for P (conditions originating in the perinatal period), and V, W, X and Y (external causes of morbidity or mortality).

Table 1: Summary of sample characteristics

N	59512
Mean EQ-5D (s.d.)	0.652 (0.321)
Mean age (s.d.)	59.00 (17.34)
Female	50.8%
Comorbidity	73.7%
Operation	73.7%
Primary ICD chapter	
A	199 (0.3%)
B	161 (0.3%)
C	4095 (6.9%)
D	2840 (4.8%)
E	1043 (1.8%)
F	100 (0.2%)
G	1530 (2.6%)
H	3479 (5.8%)
I	9284 (15.6%)
J	2643 (4.4%)
K	7771 (13.1%)
L	1671 (2.8%)
M	6837 (11.5%)
N	3781 (6.4%)
O	1005 (1.7%)
Q	148 (0.2%)
R	6494 (10.9%)

S	2120 (3.6%)
T	1420 (2.4%)
Z	2891 (4.9%)

Figure 1: Distribution of EQ-5D

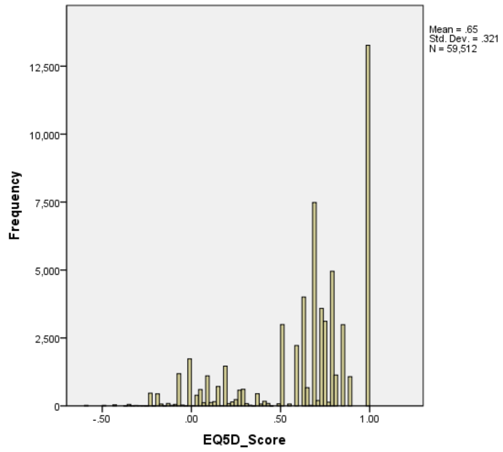


Figure 2 and Table 4 (see section 3.2) present the distribution of days the patient needed informal care, showing a huge spike at 0, smaller spikes at multiples of 5 and 7 and a large spike at 42 days (maximum number of days in the last 6 weeks).

Figure 2: Distribution of days needed care from a friend or relatives in the last 6 weeks

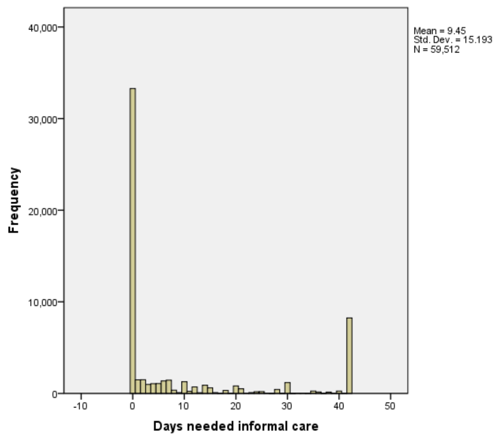


Table 2 presents the mean days the patient needed informal care by EQ-5D score. As expected the number of days increased as EQ-5D score decreased and health decreased, meaning that patients in more severe health required more informal care. Patients with an EQ-5D score of 1 had a mean of 1.46 days where they needed informal care. This was expected given that EQ-5D measures health today, whereas patients were asked to record their informal care need over the previous 6 weeks.

Table 2: Summary of days needed informal care in the last 6 weeks by EQ-5D score

EQ-5D score	Mean days (s.d.)	N
1	1.46 (5.39)	13,268
0.75≤EQ-5D<1	3.84 (9.43)	13,128
0.5≤EQ-5D<0.75	10.87 (15.64)	21,515
0.25≤EQ-5D<0.5	19.15 (18.46)	2,374
0≤EQ-5D<0.25	19.95 (18.45)	4,940
-0.25≤EQ-5D<0	27.65 (17.05)	4,106
EQ-5D<-0.25	32.90 (16.54)	181

3.2 Regression analysis

Table 3 presents regression analysis estimating informal care effects using days the patient needed informal care in the last 6 weeks. The sign and significance of the coefficients for the dummies for ICD chapters varies across the models. Coefficients had a consistent sign and were always significant for ICD chapters H and O, and for K and R (with the exception of the random effects Poisson model). EQ-5D score was negative and significant in all models as expected, meaning that as EQ-5D score increased the number of days the patient needed informal care decreased. Comorbidities were positive and significant, suggesting that patients with comorbidities required more days of informal care. The operation dummy was not always significant but was negative in the models where it was significant, meaning that it decreased the amount of days needed informal care. The sign of the coefficients for age and age-squared varied by model and the coefficients were small but generally significant. The female dummy was significant and positive (with the exception of the truncated negative binomial model of the two-part model and the zero-inflated negative binomial model) suggesting that females required more informal care even after controlling for their health and age.

Table 3: Regression output for days needed informal care in the last 6 weeks

	(1)		(2)	(3)	(4)	(5.1)	(5.2)	(6)	(7)
	Tobit	Tobit marginal effects	Poisson	RE Poisson	Negative binomial	Two-part model: Probit	Two-part model: Truncated negative binomial	Zero-inflated negative binomial, constant inflation	Zero-inflated negative binomial, variable inflation
	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$	$\hat{\boldsymbol{\beta}}$
Primary ICD chapter									
B	-5.669	-0.717	-0.173	-0.089	-0.349	-0.191	-0.143	-0.165	-0.152
	(0.248)		(0.319)	(0.261)	(0.144)	(0.290)	(0.340)	(0.286)	(0.308)
C	1.177	0.151	0.077	0.253***	-0.030	-0.006	0.037	0.039	0.040
	(0.752)		(0.536)	(0.000)	(0.857)	(0.963)	(0.689)	(0.681)	(0.657)
D	-8.719**	-1.097***	-0.254**	0.074*	-0.408**	-0.313**	-0.079	-0.109	-0.094
	(0.020)		(0.046)	(0.092)	(0.016)	(0.013)	(0.405)	(0.272)	(0.323)
E	-4.967	-0.630*	-0.079	0.098**	-0.322*	-0.250*	-0.013	-0.038	-0.021
	(0.207)		(0.549)	(0.036)	(0.075)	(0.059)	(0.895)	(0.715)	(0.834)
F	-13.754**	-1.706***	-0.467**	0.162**	-0.571*	-0.400*	-0.248	-0.278	-0.275
	(0.022)		(0.036)	(0.040)	(0.057)	(0.054)	(0.196)	(0.162)	(0.159)
G	-0.789	-0.101	0.012	0.034	-0.123	-0.063	-0.001	-0.003	0.002
	(0.836)		(0.923)	(0.449)	(0.473)	(0.624)	(0.991)	(0.979)	(0.986)
H	-11.470***	-1.436***	-0.373***	-0.196***	-0.586***	-0.370***	-0.185**	-0.229**	-0.207**
	(0.002)		(0.003)	(0.000)	(0.001)	(0.003)	(0.049)	(0.020)	(0.028)
I	-1.267	-0.162	-0.011	0.173***	-0.084	-0.062	-0.025	-0.024	-0.026
	(0.732)		(0.932)	(0.000)	(0.611)	(0.617)	(0.783)	(0.800)	(0.773)
J	-3.688	-0.469	-0.103	0.065	-0.328*	-0.128	-0.105	-0.125	-0.108
	(0.325)		(0.408)	(0.127)	(0.050)	(0.314)	(0.255)	(0.194)	(0.240)
K	-10.231***	-1.29***	-0.357***	-0.021	-0.520***	-0.312**	-0.203**	-0.237**	-0.220**
	(0.006)		(0.004)	(0.610)	(0.002)	(0.012)	(0.026)	(0.013)	(0.016)
L	-9.713**	-1.219***	-0.267**	-0.002	-0.555***	-0.345***	-0.114	-0.164	-0.128
	(0.011)		(0.039)	(0.959)	(0.001)	(0.007)	(0.241)	(0.109)	(0.186)
M	-0.783	-0.100	0.022	0.348***	-0.032	-0.012	-0.003	0.002	-0.001
	(0.832)		(0.858)	(0.000)	(0.843)	(0.922)	(0.974)	(0.982)	(0.991)
N	-7.982**	-1.007***	-0.322**	0.068	-0.416**	-0.225*	-0.226**	-0.245**	-0.236**
	(0.032)		(0.010)	(0.109)	(0.013)	(0.073)	(0.016)	(0.012)	(0.012)

	(1)		(2)	(3)	(4)	(5.1)	(5.2)	(6)	(7)
O	-9.896***	-1.240***	-0.764***	-0.465***	-0.809***	-0.323**	-0.537***	-0.617***	-0.559***
	(0.010)		(0.000)	(0.000)	(0.000)	(0.014)	(0.000)	(0.000)	(0.000)
Q	1.756	0.226	0.087	0.224**	-0.043	0.054	-0.009	0.003	-0.004
	(0.718)		(0.635)	(0.022)	(0.845)	(0.756)	(0.952)	(0.985)	(0.978)
R	-11.896***	-1.492***	-0.347***	0.015	-0.636***	-0.386***	-0.189**	-0.232**	-0.208**
	(0.001)		(0.005)	(0.714)	(0.000)	(0.002)	(0.039)	(0.015)	(0.023)
S	8.338**	1.083***	0.297**	0.511***	0.323*	0.251**	0.137	0.161*	0.148
	(0.026)		(0.017)	(0.000)	(0.053)	(0.048)	(0.135)	(0.095)	(0.106)
T	0.525	0.067	0.079	0.245***	0.022	-0.044	0.069	0.068	0.069
	(0.891)		(0.527)	(0.000)	(0.899)	(0.733)	(0.456)	(0.486)	(0.457)
Z	-11.662***	-1.458***	-0.329***	-0.091**	-0.676***	-0.445***	-0.092	-0.154	-0.113
	(0.002)		(0.010)	(0.037)	(0.000)	(0.000)	(0.327)	(0.119)	(0.228)
EQ-5D score	-65.121***	-8.339***	-1.891***	-1.130***	-2.829***	-2.205***	-0.870***	-1.028***	-0.858***
	(0.000)		(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Comorbidity	5.988***	0.762***	0.279***	0.148***	0.339***	0.169***	0.152***	0.186***	0.148***
	(0.000)		(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Operation	-1.310***	-0.168***	-0.014	0.005	-0.077***	-0.074***	0.013	0.004	0.009
	(0.002)		(0.351)	(0.440)	(0.001)	(0.000)	(0.304)	(0.782)	(0.504)
Age	-0.431***	-0.055***	0.000	-0.011***	-0.007*	-0.025***	0.019***	0.017***	0.019***
	(0.000)		(0.846)	(0.001)	(0.051)	(0.000)	(0.000)	(0.000)	(0.000)
Age-squared	0.004***	0.001***	0.000*	0.000***	0.000***	0.000***	-0.000***	-0.000***	-0.000***
	(0.000)		(0.060)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Female	7.352***	0.941***	0.170***	0.261***	0.313***	0.334***	-0.022*	0.011	-0.023*
	(0.000)		(0.000)	(0.000)	(0.000)	(0.000)	(0.070)	(0.374)	(0.061)
Constant	42.796***		2.882***	2.182***	3.609***	1.887***	2.671***	2.737***	2.654***
	(0.000)		(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Inflated variables								$\hat{\gamma}$	$\hat{\gamma}$
Constant								0.125***	-3.343***
								(0.000)	(0.000)
EQ-5D score									4.123***
									(0.000)

	(1)		(2)	(3)	(4)	(5.1)	(5.2)	(6)	(7)
Comorbidity									-0.393***
									(0.000)
Age									0.048***
									(0.000)
Age-squared									-0.000***
									(0.000)
Female									-0.563***
									(0.000)
Dispersion (α)					5.124		0.796	0.875	0.821
					(0.049)		(0.010)	(0.014)	(0.012)
Observations	59512		59512	59512	59512	59512	26240	59512	59512
Number of patients				44494					

Notes: p values in parentheses. * significant at 10%; ** significant at 5%; *** significant at 1%

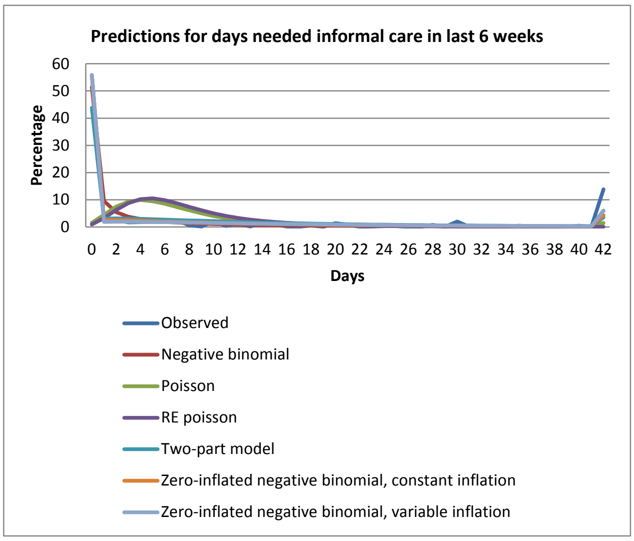
Table 4 and Figure 3 present predictions of days needed care for the estimated models with the exception of the Tobit model. The generated predictions are the mean proportions of the population with a predicted given number of days, estimated using the mean probability across all individuals of the predicted probability for each given number of days. These predictions are presented to enable a comparison of how well each model predicted the observed distribution of days needed informal care. The negative binomial and the zero-inflated negative binomial were the best models at predicting. Overall the zero-inflated negative binomial with variable inflation most accurately predicted the spikes at 0 days and 42 days. Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) (not reported) both selected the zero-inflated negative binomial with variable inflation over the negative binomial model. The Poisson and random effects Poisson models were poor at estimating the large spike at 0 days, with the predictions instead forming a lower tail from 1 to 14 days which did not reflect the observed distribution. Additionally, there was no spike at 42 days. The Poisson model is appropriate when the mean and variance were similar, yet the distribution of days needed informal care suffered from overdispersion, where the variance was much larger than the mean. The two-part model more accurately predicted the spikes at 0 days and 42 days than the Poisson models, but still had a thicker lower tail of predictions.

Table 4: Predictions of days needed informal care in the last 6 weeks

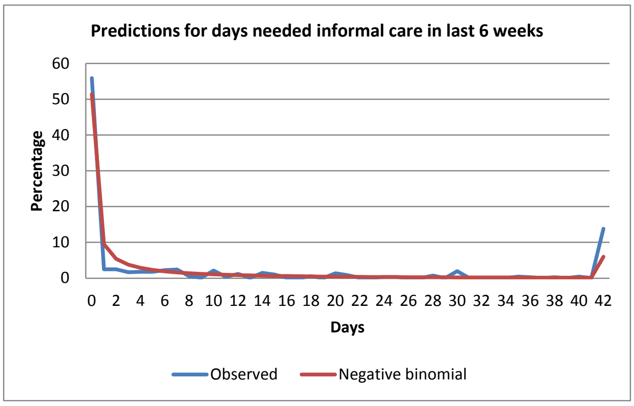
Days	Observed Frequency	Observed Percent	Poisson	RE Poisson	Two-part model	Negative binomial	Zero-inflated negative binomial, constant inflation	Zero-inflated negative binomial, variable inflation
0	33272	55.91	1.50	0.91	43.84	51.41	55.55	55.78
1-7	8887	14.94	56.39	57.39	20.21	27.39	15.64	12.53
8-14	3615	6.07	24.50	30.66	13.88	6.95	10.14	9.49
15-21	2388	4.01	7.44	7.99	8.53	3.56	6.32	6.60
22-28	971	1.64	4.63	2.25	5.17	2.19	4.00	4.54
29-35	1542	2.60	2.77	0.57	3.14	1.48	2.60	3.14
36-41	592	1.01	1.29	0.14	1.70	0.94	1.51	1.93
42	8245	13.85	1.47	0.08	3.50	6.00	4.26	6.00

Figure 3: Predictions of days needed informal care in the last 6 weeks

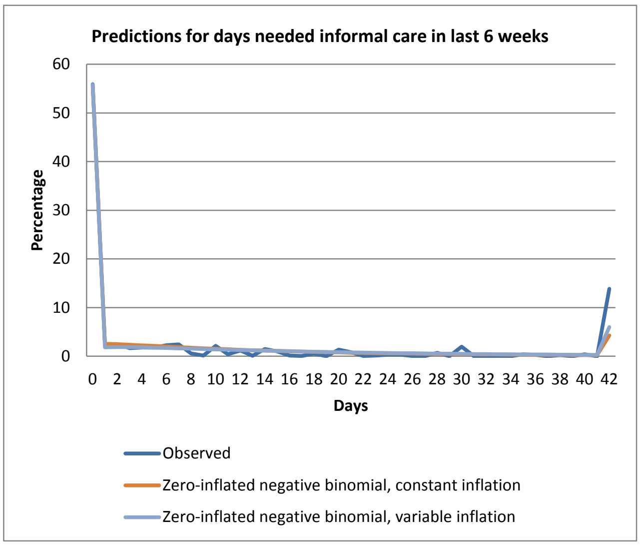
a) All models



b) Negative binomial

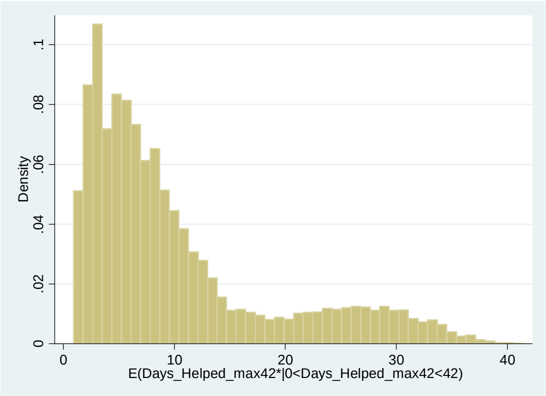


c) Zero-inflated negative binomial



The Tobit model predictions cannot be presented in this way as the model does not generate probabilities, but instead generates the number of days as a continuous variable. Figure 4 presents the distribution of the Tobit predictions, illustrating that it did not accurately predict the spike at 0 days and instead had a positively skewed distribution, and did not predict the spike at 42 days.

Figure 4: Distribution of Tobit model predictions for days needed informal care in the last 6 weeks



The specification of the model with the most accurate predictions, the zero-inflated negative binomial with variable inflation, was explored by excluding the comorbidity and operation variables and insignificant ICD chapters (see Appendix). The comorbidity and operation variables were excluded as these may not always be available in datasets used in economic evaluation, although it should be recognised that this lack of data may lead to biased estimates. An additional set of analyses was also undertaken by excluding statistically insignificant ICD chapters to obtain a more parsimonious model, although AIC and BIC indicated that the original specification of the model was preferred. There was also little variation in days predicted across these regressions and these additional models did not improve predictive performance.

4 DISCUSSION

4.1 Summary

This report has presented regression analyses that enables the estimation of informal care associated with the health of the patient. These analyses enabled the prediction of days the patient needed informal care in the last 6 weeks using the health and sociodemographic characteristics of the patient. The linkage between EQ-5D and ICD chapter with informal care time enabled the measurement of the impact of medicines on carer time via their impact on health. The estimate of days can then be converted into a cost value using available methods in the existing literature and used in economic evaluation of health interventions. Such an approach is much simpler than the alternative approaches that have been used in evaluations to date, which have collected care data for the relevant patient-carer population.[6]

4.2 Modelling the data

The distribution of days the patient needed informal care provided a variety of challenges for the regression analysis, with a very large spike at 0 days, spikes at multiples of 5 and 7 days and a large spike at 42 days. A variety of different regression models were estimated that are appropriate for the type and distribution of the data. The Poisson model was poor at predicting the number of days, and taking into account repeated observations at the individual level using the random effects Poisson model did not improve these predictions. The two-part model was much better at predicting, but still under predicted the very large spike at 0 days. The negative binomial and zero-inflated negative binomial models were consistently the best models at predicting the distribution of the number of days and were capable of describing the spikes at zero and 42 days. Not surprisingly, none of the models were able to accommodate the multiple spikes at multiples of 5 and 7 days.

The choice of preferred model between the negative binomial, zero-inflated negative binomial model with constant inflation and the zero-inflated negative binomial model with variable inflation needs to take into account their econometric performance. The zero-inflated negative binomial model with variable inflation was best overall at predicting both the spike at 42 days, which represented a large informal care cost as these individuals required informal care every day in the last 6 weeks, and the very large spike at 0 days, which represented zero informal care. The negative binomial model in contrast predicted the spike at 42 days but under predicted the spike at 0 days, and the reverse was found for the zero-inflated negative binomial model with constant inflation. However, between around 5 and 41 days all models over predicted the number of days, with this over prediction being least for the negative binomial and greatest in the zero-inflated negative binomial model with variable inflation. This over prediction was possibly a consequence of the spike at 42 days which none of the models can fully capture, and as a result, this distorts the estimated distribution in the tail. Given that the spike appears to be partly an artefact of imprecise survey responses (as discussed below), this over prediction/distortion may have represented a bias in estimated value in this range.

Model choice should also consider the decision making context within which the predictions will be made. If a model fits well overall, but is poor at describing an important part of the distribution, then this should be taken into consideration. For this patient population, accurate predictions of the observations at zero and 42 days was very important as these accounted for almost 70% of the observations. Having considered both the fit of the models and the decision making context within which the models will be applied, the zero-inflated negative binomial model with variable inflation was considered to be the most relevant. By way of example, the Appendix gives the estimated equation needed to calculate the number of days of informal care based on model (7) and a 60-year old female patient within ICD Chapter B, with no comorbidities or recent operation.

The relationship between EQ-5D and informal care was consistent and significant, where lower EQ-5D score meant higher informal care. Patients with comorbidities also consistently and significantly had higher informal care. The relationship between whether the patient had an operation and informal care was not as clear, but generally indicated that having an operation reduced the number of days they needed informal care. These effects may be observed because following an operation the patient is more able to look after themselves than patients whose treatment did not or could not involve an operation, yet this is contrary to what may be expected. Alternatively the reduction of informal care following an operation may be due to an increase in formal care, for example through home visits by nurses or social services. The relationship between ICD chapter and informal care was not as clear. The sign and significance of the dummies for ICD chapter varied across models and for the different dependent variables. Exclusion of comorbidity and operation variables and insignificant ICD chapters from the full specification produced a deterioration in model performance (as indicated using AIC and BIC statistics), but had little impact on days predicted. The sign and significance of age and age-squared varied. Being female significantly increased the number of days needed informal care.

The analyses built upon the approach taken by Dixon et al (2006),[12] using the same dataset but with additional observations (additional years of data) and regression models that were more appropriate for the data. Different model specifications were estimated here as Dixon et al focussed upon the use of dummy variables for the severity levels of each EQ-5D dimension rather than the utility score and did not incorporate ICD chapter or other health variables into their models. Dixon et al found that using severity levels produced better models, but such models were not explored here as their applicability is limited because analysts rarely have access to patient level data. The results were consistent, with improvements in the health of the patient meaning reduced informal care, but contrary to our results Dixon et al found that being female significantly reduced the number of days needed informal care.

4.3 Limitations

One limitation of the analyses undertaken here is that they will not be appropriate for predicting informal care when either EQ-5D is inappropriate for the patient population or when the relationship between EQ-5D and days needed informal care is inappropriate for the patient population. The analyses may also be less reliable for the ICD chapters where there are fewer observations as the relationship is based on a smaller sample.

A further limitation of this study is that the dependent variable was generated from a question asking patients to recall how many days a friend or relative had needed to provide care or help them with normal activities in the last six weeks. It is well documented that questions of recall may be prone to bias and potentially systematic error. This may be exacerbated by the six week recall period, as recalling care or help needed over the last six weeks is a difficult task. Potential problems with the data are illustrated by the fact that raw observations had a maximum of 45 days and spikes at multiples of 5 and 7 days, suggesting that respondents were approximating the number of days using weeks or months (for example, 6 weeks may be converted into one and a half months, which is approximately 30+15=45 days). Although the spikes at multiples of 5 and 7 days were not altered, responses of greater than 42 days were truncated at 42 days because this may have reflected a real propensity for carers to plan their input in terms of whole weeks. Alternative approaches to treating both of these issues are possible.

Whilst the recall period of the informal care question in HODaR may be an issue, the framing of the question in terms of ‘friends and relatives’ overcomes one problem with previous studies which have often focused on the primary caregiver. Neubauer and colleagues[15] have shown that estimating the time of the primary care giver can produce a substantial underestimate of the costs of informal care.

Another issue relates to the underlying patient population within HODaR. The vast majority of patients were recently discharged from hospital, and as such, were not in a stable health state. In addition, the EQ-5D captured the health of the patient at a single point at the end of the 6 week recall period. Consequently, a patient with a low EQ-5D on discharge (with informal care needs) could recover to full health (with no informal care needs) by the time they complete the EQ-5D at six weeks. This could lead to a systematic overestimation of the informal care needs for relatively mild health states.

Another limitation is that the analyses were based primarily on cross-sectional data with few repeated observations across individuals. Consequently, the relationship between health and informal care may not hold when changes in EQ-5D values over time are considered, which is a central issue in cost-effectiveness analysis. A further limitation is that the dataset excluded people with a primary diagnosis on admission of a psychological illness or learning disability and therefore is not recommended for use in health interventions for these patients. Furthermore the sample may suffer from response bias as only respondents with complete data on the variables used in the models were analysed.

The most straightforward and inexpensive method of providing a monetary valuation of the days of informal care is to use existing values in the literature for specified tasks or hours. However the dependent variable creates challenges for the monetary valuation of the number of days of informal care as the HODaR dataset does not include data on the number of hours in each day that the patient required informal care or the tasks that were undertaken during that time. There is no guidance on how to convert days into hours and tasks or which monetary values to use from the literature. Further research is encouraged in this area.

5 CONCLUSION

This paper has shown that patients with lower EQ-5D scores have higher informal care need than patients with higher EQ-5D scores. The preferred regression model estimated here can be used to predict changes in informal care associated with changes in the health of the patient, measured using EQ-5D. This information can be used to inform economic evaluation of health interventions. The main limitations of this study relate to the underlying dataset, in particular, exclusions of some patient groups from the patient population and the imprecision of measurement. If a dataset can be generated that overcomes these issues, arguably the analysis presented here has shown that a robust relationship between patient EQ-5D tariff values and informal care time can be estimated. Such an approach has many advantages over the direct measurement of informal care in each individual patient population, although the degree of imprecision introduced by estimation rather than observation is currently unknown. It is recommended that future research should specify and generate a more appropriate dataset for re-estimating the relationship between EQ-5D utility scores and amount of informal care. This relationship should then be used in studies that have collected informal care time data, so that the differences between the two methods can be calculated and a preferred method – in terms of accuracy and practicability – identified.

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7 Appendix

Table A1: Regression output for days needed informal care in the last 6 weeks using the zero-inflated negative binomial, variable inflation

	(7)	(8)	(9)
	Full specification	Excluding comorbidity and operation	Excluding comorbidity, operation and insignificant ICD chapters
	$\hat{\beta}$	$\hat{\beta}$	$\hat{\beta}$
Primary ICD chapter			
B	-0.1521227	-0.1637413	
	(0.308)	(0.267)	
C	0.0404685	0.0653931	
	(0.657)	(0.470)	
D	-0.0935055	-0.0781314	
	(0.323)	(0.405)	
E	-0.0209114	-0.0447061	
	(0.834)	(0.653)	
F	-0.2746472	-0.2684327	
	(0.159)	(0.168)	
G	0.0016516	-0.0181693	
	(0.986)	(0.847)	
H	-0.2065952**	-0.2638745***	-0.2413849***
	(0.028)	(0.005)	(0.000)
I	-0.0260221	-0.0199258	
	(0.773)	(0.824)	
J	-0.1084329	-0.1124996	
	(0.240)	(0.220)	
K	-0.2202850**	-0.2373998***	-0.2150041***
	(0.016)	(0.009)	(0.000)
L	-0.1284655	-0.1587337	-0.1353630***
	(0.186)	(0.101)	(0.001)
M	-0.0010566	-0.0233951	
	(0.991)	(0.794)	
N	-0.2357236**	-0.2525494***	-0.2306172***
	(0.012)	(0.006)	(0.000)
O	-0.5592390***	-0.5897744***	-0.5652293***
	(0.000)	(0.000)	(0.000)
Q	-0.0041634	-0.0013532	
	(0.978)	(0.993)	
R	-0.2076075**	-0.2150206**	-0.1921381***
	(0.023)	(0.018)	(0.000)
S	0.1483263	0.1724565*	0.1954825***
	(0.106)	(0.058)	(0.000)
T	0.0690814	0.0827777	
	(0.457)	(0.370)	

	(7)	(8)	(9)
Z	-0.1132731	-0.1223117	
	(0.228)	(0.190)	
EQ-5D score	-0.8583409***	-0.8615388***	-0.8568926***
	(0.000)	(0.000)	(0.000)
Comorbidity	0.1478759***		
	(0.000)		
Operation	0.0088101		
	(0.504)		
Age	0.0194834***	0.0202336***	0.0211118***
	(0.000)	(0.000)	(0.000)
Age squared	-0.0001203***	-0.0001228***	-0.0001303***
	(0.000)	(0.000)	(0.000)
Female	-0.0226854*	-0.0250989**	-0.0244492**
	(0.061)	(0.039)	(0.041)
Constant	2.6540856***	2.7521391***	2.7035928***
	(0.000)	(0.000)	(0.000)
Inflated variables	$\hat{\gamma}$	$\hat{\gamma}$	$\hat{\gamma}$
Constant	-3.342591***	-3.570886***	-3.572268***
	(0.000)	(0.000)	(0.000)
EQ-5D score	4.122554***	4.171449***	4.17282***
	(0.000)	(0.000)	(0.000)
Comorbidity	-0.3932173***		
	(0.000)		
Age	0.0482827***	0.0458967***	0.0459329***
	(0.000)	(0.000)	(0.000)
Age-squared	-0.0004012***	-0.0003929***	-0.0003933***
	(0.000)	(0.000)	(0.000)
Female	-0.56294***	-0.5482281***	-0.5482189***
	(0.000)	(0.000)	(0.000)
Dispersion (α)	0.8205201	0.8273329	0.8287567
	(0.012)	(0.012)	(0.012)
Observations	59512	59512	59512
No. of patients	44494	44494	44494
Log likelihood	-136934	-137131	-137161
AIC	4.603	4.610	4.610
BIC	-380040	-379678	-379752

Table A2: Predictions for days needed informal care in the last 6 weeks using the zero-inflated negative binomial, variable inflation

Days	Frequency	Percent	(7) Full specification	(8) Excluding comorbidity and operation	(9) Excluding comorbidity, operation and insignificant ICD chapters
0	33272	55.91	55.78	55.77	55.77
1 to 7	8887	14.94	12.53	12.6	12.56
8 to 14	3615	6.07	9.49	9.49	9.48
15-21	2388	4.01	6.60	6.60	6.60
22-28	971	1.64	4.54	4.53	4.54
29-35	1542	2.60	3.14	3.13	3.14
36-41	592	1.01	1.93	1.92	1.93
42	8245	13.85	6.00	5.99	6.00

Example of calculation of predicted number of days of informal care using model (7)

Calculation of the number of days of informal care based on model (7) for a 60-year old female patient within ICD Chapter B, with no comorbidities or recent operation.

Using equation (7):

$$E(y_i \mid \mathbf{x}_i, \mathbf{z}_i) = \left(1 - \frac{e^{\mathbf{z}_i^{'}\boldsymbol{\gamma}}}{1 + e^{\mathbf{z}_i^{'}\boldsymbol{\gamma}}}\right) e^{\mathbf{x}_i^{'}\boldsymbol{\beta}}$$

$$= \left(1 - \frac{e^{-3.342591+4.122554EQ5D+0.0482827*60-0.0004012*60*60-0.56294}}{1+e^{-3.342591+4.122554EQ5D+0.0482827*60-0.0004012*60*60-0.56294}}\right) e^{2.6540856-0.1521227-0.8583409EQ5D+0.0194834*60-0.0001203*60*60-0.0226854}$$

If EQ-5D=0.5:

$$= \left(1 - \frac{e^{-3.342591+4.122554*0.5+0.0482827*60-0.0004012*60*60-0.56294}}{1+e^{-3.342591+4.122554*0.5+0.0482827*60-0.0004012*60*60-0.56294}}\right) e^{2.6540856-0.1521227-0.8583409*0.5+0.0194834*60-0.0001203*60*60-0.0226854}$$

$$= \left(1 - \frac{e^{-0.391612}}{1+e^{-0.391612}}\right) e^{2.7860315}$$

$= 9.68$ days