Quantifying Uncertainty in Long-term Care Costs following the Introduction of New Drug Therapy

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1. Introduction

Guidance on resource allocation decisions in health care is increasingly relying on cost-effectiveness evidence. Whilst economic evaluation methods assist in such decisions, they fail to provide information on the affordability of particular forms of health care. This is likely to be a concern for policy-makers concerned with guidance implementation, as there may be a positive link between affordability and implementation.

Methods known as Budget Impact Analyses have been developed to address affordability questions (Chambers et al. 2002). These are now being used in a number of countries to inform decision-making (Trueman et al. 2001). The Australian Pharmaceutical Benefits Advisory Committee, the National Institute for Health and Clinical Excellence (NICE) in the UK and the Sickness Funds Council in the Netherlands all recommend that health care system costs should be estimated in any reimbursement submissions.

Previous estimates of budget impact for NICE have largely been undertaken using deterministic methods (NICE 2001). It is unclear how reliable or uncertain these estimates are. However, using probabilistic sensitivity analysis methods (Briggs 2000), quantification of the uncertainty around budget impact estimates is also possible using regression modeling of cost data (Barber and Thompson 2004).

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Using Ordinary Least Squares (OLS) and Generalized Linear Model (GLM) estimation, this paper compares the results from both methods with previous NICE deterministic estimates that quantified the net long-term care costs of cholinesterase inhibitor therapy for Alzheimer's disease (AD) to the health and social care system in England and Wales.

2. Methods

Budget impact of therapy was estimated using cohort simulation modelling using a ten year time horizon. The cohort comprised the current AD population in England and Wales, based on 2002 national population estimates (NATIONAL STATISTICS 2004) and AD prevalence rates (MRC CFAS 1998). The effects of therapy on cognition were applied to the cohort using estimates obtained from a systematic review of clinical effectiveness (BIRKS and HARVEY 2004), observational data (LOPEZ et al. 2002) and natural history studies (MUNGAS et al. 2001; NEALE et al. 2001). The relationship between cognition and costs was estimated using GLM regression, with costs modelled as a function of age, gender, Mini-Mental State Examination (MMSE) score and Activities of Daily Living (ADL) score, using data from a previous observational multi-centre study (MCNAMEE et al. 1999). To compare the results with previous estimates (NICE 2001), the model was constructed so that only patients with a level of MMSE greater than 12 commenced therapy and were withdrawn from therapy when MMSE was no longer greater than 12. Baseline assumptions for model parameters are outlined in Table 1.

The sensitivity of the results to different model assumptions was assessed using probabilistic sensitivity analysis. This involved taking repeated random draws from specific distributions of key parameters (MMSE and ADL baseline values, MMSE change per year, survival, regression coefficients). The correlation between parameters was modelled using Cholesky decomposition based on variance-covariance matrix values.

The modelling strategy compared a GLM with an identity-link function and Gaussian distribution (i.e. untransformed OLS) with alternative GLMs that possessed different link functions and distributions.

Table 1: Model Assumptions and Parameters

Parameter	Value/assumption	Data Source
Population of England and Wales aged 65 years or over in mid 2002	8,385,800	National Statistics (2004)
Prevalence of AD	50% of age and sex specific rates for dementia	MRC CFAS (1998)
Cohort distribution by baseline MMSE	Age and sex specific values from a minimum of 12.7 to a maximum of 18.6	McNamee et al. (1999)
Cohort distribution by baseline ADL	Age and sex specific values from a minimum of 6.5 to a maximum of 13.8	McNamee et al. (1999)
Cohort distribution by baseline costs per person per year	Age and sex specific values from a minimum of £1584 to a maximum of £14,457	McNamee et al. (1999)
MMSE reduction per year without therapy	Age specific values from a minimum of 2 to a maximum of 3	Mungas et al. (2001)
MMSE reduction per year with therapy	Age specific values from a minimum of 1.2 to a maximum of 1.8	Lopez et al. (2002)
Therapy costs per person per year	£891	British National Formulary (2003)
Cost savings per person per year per MMSE point reduction (OLS)	£414	Regression estimates
Cost savings per person per year per MMSE point reduction (GLM)	£343	Regression estimates
Discount rate	3.5%	Treasury Green Book (2003)
Survival probability to 1, 3 and 5 years	Age, sex and time varying values from a minimum of 0.18 to 0.90	Neale et al. (2001)

Table 2: Comparison of OLS and GLM Estimated Incremental Costs per Patient over 10 Years

OLS values (£)		GLM values (£)		% difference
Deterministic	596.7916	Deterministic	736.5616	0.234202
Probabilistic	607.3662	Probabilistic	333.7527	–0.45049

Table 3: Comparison of Alternative GLM Estimators

Model	Constant	Sex	Age	ADL	MMSE	AIC	Bias*
Identity link							
Gaussian	–1.13 (151.25)	–49.77 (22.60)	5.35 (1.66)	–9.98 (1.90)	–7.96 (2.46)	13.47	0.26
Poisson**	–	–	–	–	–	–	–
Gamma	–42.58 (0.00)	–10.88 (0.00)	1.82 (0.00)	–3.46 (0.00)	–0.94 (0.00)	1.16e + 8	0.78
Negative binomial	231.47 (100.84)	–6.95 (12.32)	1.55 (0.94)	–7.62 (1.25)	–7.12 (1.53)	11.89	0.31
Log link							
Gaussian	2.88 (0.90)	–0.35 (0.12)	0.04 (0.01)	–0.06 (0.01)	–0.03 (0.01)	13.46	0.26
Poisson	3.72 (0.06)	–0.32 (0.01)	0.04 (0.00)	–0.06 (0.00)	–0.05 (0.00)	213.09	0.26
Gamma	4.37 (1.02)	–0.44 (0.16)	0.04 (0.01)	–0.06 (0.01)	–0.09 (0.02)	11.85	0.21
Negative binomial	4.37 (0.73)	–0.44 (0.12)	0.04 (0.01)	–0.06 (0.01)	–0.09 (0.01)	11.86	0.21

* Computed as the absolute value of the difference between mean predicted and mean actual weekly costs divided by mean actual weekly costs

** Convergence not achieved

Variable definitions: *Sex* (= 1 if female, = 0 if male); *Age* (years); *ADL* (Activities of Daily Living index, range 0–18, scored according to whether respondents required help (= 0), have problems (= 1) or have no difficulties with (= 2) nine daily activities); *MMSE* (Mini Mental State Examination index, range 0–30, where values 0–10, 11–22 and 23–30 indicate severe, moderate to mild, and absence of cognitive impairment respectively).

Standard errors in parentheses.

3. Results

Using deterministic OLS analysis, mean discounted net care costs were £115 million, or £597 per patient over 10 years. Table 2 shows that the probabilistic sensitivity analysis supported the findings from the OLS deterministic model that treatment did not produce cost savings large enough to offset the costs of therapy. Table 2 also shows however that the deterministic GLM model produced a mean incremental cost estimate that was 23% *higher* than the OLS model, whilst the probabilistic GLM estimate was 45% *lower* than the OLS model.

Table 3 shows the performance of alternative GLM estimators. Based on low AIC values, amongst log-link versions there was little to choose between alternative distributional forms. A Park test value of 1.25 suggests that both the negative-binomial and gamma distributions are appropriate (Manning and Mullahy 2001).

Figures 1 and 2 provide information relating to the range surrounding the mean estimates. They show that the GLM probabilistic model has more extreme values than the OLS model. This gave rise to greater uncertainty within GLM estimates over the likelihood of therapy producing net savings. With OLS, the probability that therapy was cost saving was zero. With GLM, this probability equalled 0.212.

4. Discussion

The analyses in this paper suggest that the introduction of cholinesterase inhibitors is likely to lead to additional costs from the perspective of the health and social care systems of England and Wales. The estimated magnitude of these additional costs is different from previous NICE guidance (NICE 2001), which computed a figure of £42 million per year. The modelling approach was also demonstrated to be important, as the probability that therapy was cost saving was considerably different in GLM estimation.

Where estimates are a linear function of covariates on the log-link scale, a previous study showed that outliers greatly affect GLM parameter estimates (Blough and Ramsey 2000). This suggests that probabilistic analysis using the multiplicative GLM is more sensitive to less precise estimates. This leads to greater error propagation as GLM estimates are calculated using the product of the exponentiated coefficients. This is not problematic if the values appear credible. However, for a one point reduction in MMSE, the higher values generated by GLM appear less valid than the lower values produced by OLS. For example,

Figure 1: OLS Estimate of Incremental Costs per Cohort over Ten Years

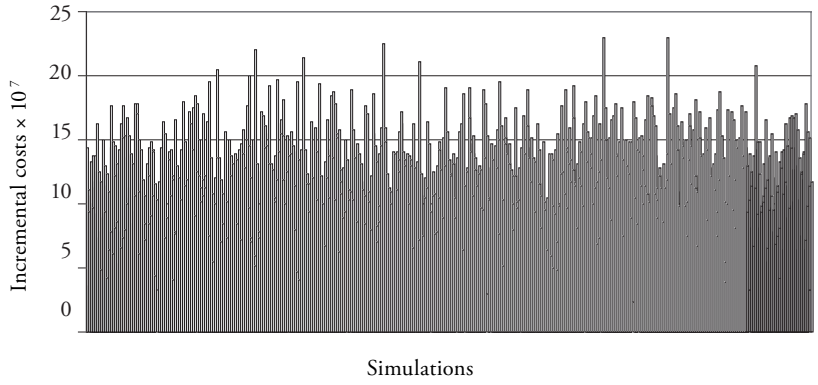
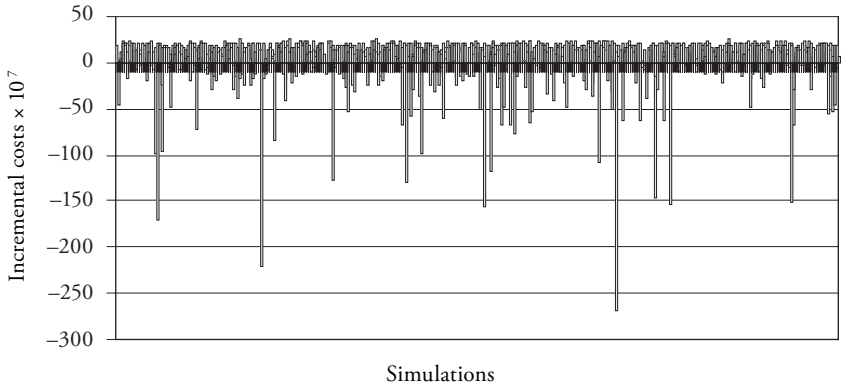


Figure 2: GLM Estimate of Incremental Costs per Cohort over Ten Years



in some simulations a saving of £3000 per year per MMSE point reduction is produced from GLM estimation. This implies a saving of approximately 2 months in long-stay residential care, which has not been demonstrated in previous clinical trials (AD2000 COLLABORATIVE GROUP 2004).

In conclusion, calculation of the uncertainty surrounding budget impact estimates may help to inform policy guidance decisions. The analytical approach

used can take a variety of forms. This paper demonstrates that probabilistic methods based on regression techniques can be employed to generate such estimates. However, where results are sensitive to the modelling approach adopted, careful attention to the validity of the resulting estimates is required.

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