Inpatient and non-inpatient resource utilization of type-2 diabetes patients

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Abstract:

Reliable estimates of the impact of complications on resource use and healthcare costs are important for researchers studying cost-effectiveness of interventions. We provide new estimates of the cost of diabetes complications using 10 years of additional data from the landmark UK Prospective Diabetes Study (UKPDS). We analyse inpatient and non-inpatient utilisation between 1997 and 2007 for the 3161 English patients who continued in the Post Trial Monitoring phase, using hospitalization records for England and questionnaires administered annually to patients requesting information on home, clinic, and telephone contacts with general practitioners, nurses, podiatrists, opticians, and dieticians, eye and other hospital out-patient clinics.

We estimated the immediate and long term impact on inpatient and non-inpatient costs of myocardial infarction, ischemic heart disease, stroke, heart failure, amputation, blindness in one eye, and retinal photocoagulation, controlling for patient specific characteristics. The results reported in this paper are expected to be representative of an older diabetic population.

The likelihood of hospitalization increased from 6% to 14% in the absence of diabetes related complications. The estimated unconditional inpatient cost of first complications were as follows: amputation £8,222 (95% confidence interval £6799, £10146); nonfatal myocardial infarction £2759 (£1927, £3534); fatal myocardial infarction £522 (£312, £742); fatal CHF £320 (£86, £711); non-fatal stroke £1845 (£1222, £2552); non-fatal ischemic heart disease £3460 (£2631, £4101); fatal ischemic heart disease £382 (£212, £616); heart failure £2000 (£3390, £2852); cataract extraction £1963 (£1500, £2681); and blindness in one eye £638 (£297, £924). The annual average in-patient cost of events having had a history of diabetes related complication in subsequent years was significantly lower than the costs incurred during the year of the complication, ranging from £414 for patients who had had cataract extraction to £1476 for patients with a history of amputations. These costs however were higher than those incurred by patients who were free of complications.

Non-inpatient costs for amputation were £1320 (95% confidence interval £1001, £1535); nonfatal myocardial infarction £933 (£767, £1106); non-fatal stroke £926 (£792, £1203); non-fatal ischemic heart disease £744 (£592, £860); heart failure £792 (£631, £969); cataract extraction £625 (£545, £723); and blindness in one eye £962 (£735, £1476) in the year of the event. In each subsequent year, non-inpatient costs ranged from £640 for IHD to £1345 for amputations. For patients having no complications, routine non-inpatient care costs increased by 54% over the 10-year follow-up, and particularly between 1997 and 2003. This period corresponded with the publication of UKPDS results demonstrating the benefits of intensive therapy and the subsequent changes in treatment guidance and protocols.

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1- Introduction

Reliable estimates of the impact of complications on resource use and healthcare costs are important for researchers studying cost-effectiveness of interventions. We provide new estimates of the cost of diabetes complications using 10 years of additional data from the landmark UK Prospective Diabetes Study (UKPDS). In-patient costs are estimated using multiple regression analysis based on costs calculated from Healthcare Resource Groups (HRG) on all English patients who entered the Post Trial Monitoring phase of the study in 1997, and non-inpatient costs are estimated using annual questionnaires sent to the same patients.

The study builds on previous work by Clarke, Gray et al. (2003) who used information on hospital in-patient stays and occurrence of complications collected during 4-monthly UKPDS clinic visit, and information on non-inpatient resource utilization based on a single cross-sectional survey. From these sources, estimates were made of the effects of 7 pre-specified clinical events (non fatal and fatal myocardial infarction (MI), ischemic heart disease (IHD), fatal and non-fatal stroke, heart failure, amputation, cataract extraction and blindness) on health care costs. 10 additional years of follow-up data are now available, including 5 more waves of questionnaire, permitting re-estimation and validation of the results previously reported.

Previously, for inpatient costing, inpatient episodes were costed by obtaining information on the specialty in which the admission occurred, and then attaching a specialty-specific cost per inpatient day using information from Trust Financial Returns (TFR2). That approach was relatively simple to implement but also had limitations. For instance, attaching a flat rate per day to the number of bed days may not reflect accurately the cost of a hospitalization, as it is likely that the bulk of costs fall at the beginning of the hospitalization period. Similarly, the costs of treating an uncomplicated fracture could be different from the treatment of a complicated fracture in an elderly diabetic patient, while the cost of dialysis for a patient without co-morbidities is likely to be considerably lower than the cost of dialysis if the patient has co-morbidities (Zsolt and Smith, 2005). To address these issues, we now use an HRG-based method to cost admissions (HRG4), taking into account not only specialty and length of stay but also other characteristics of the patient and the admission.

It important to go beyond pure accounting costs, i.e. healthcare costs that are administratively allocated to events (e.g. the average cost of an in-patient admission for a MI) for two main reasons: First, we want to be able to estimate the increase in all healthcare costs in the year in which the complication occurs and on patients having a history of one or more conditions. Second, average costs mask a lot of patient heterogeneity: the underlying level of healthcare

utilization or inpatient admissions is a phenomenon endogenous to the patient and his/her characteristics and we want to disentangle this from the cost of the complication itself.

The following section outlines the data used. The modelling strategy is presented in section 3. The results section presents the cost of inpatient and outpatient care across a set of diabetes-related complications, looking at the immediate and the longer-term effects of these complications on both types of resource utilization, and finally, in the conclusion we summarize our findings and suggest possible avenues for future research.

2- Data

We use patient level data from the UK Prospective Diabetes Study (UKPDS), a landmark randomized trial of glycaemic therapies in 5,102 newly diagnosed patients with no existing serious complication at diagnosis. The trial ran for 20 years from 1977 to 1997 in 23 centres across the UK. From September 1997 the intervention phase of the study closed and the 4,189 surviving patients were treated to best practice by their GPs. At that point patients entered a post-trial monitoring study, which continued to collect information on clinical events and resource use until 2007. Details of the study design and the main clinical results have been published elsewhere (UKPDS(33), 1998, UKPDS(34), 1998, UKPDS(38), 1998).

Inpatient episodes

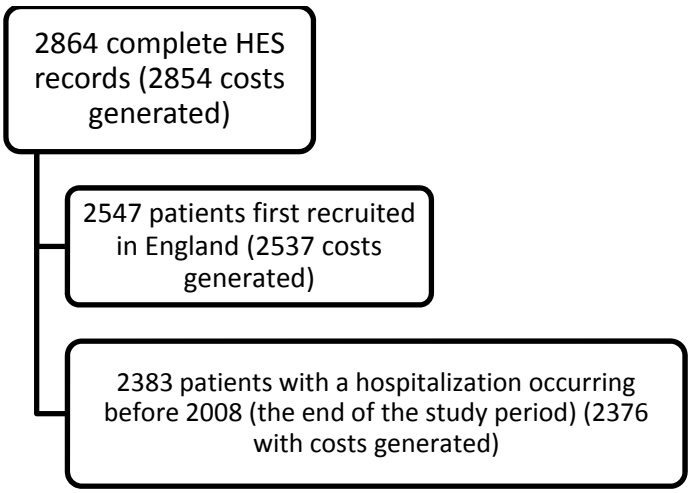
Information on hospital inpatient use was obtained from Hospital Episode Statistics (HES), the English national statistical data warehouse for hospital use, matching records to patients recruited to the UKPDS trial using encrypted NHS numbers. Diabetes related endpoints were recorded during routine (4-monthly) visits to UKPDS clinics, and adjudicated by an endpoint committee. These datasets were then combined to estimate the impact of diabetes related complications on inpatient resource usage and on costs.

Of the initial 5,102 patients recruited to the UKPDS trial, 1,724 (24.75%) did not live in England (1,263 in Scotland and 461 in Northern Ireland). Scottish and Northern Irish survivors in 1996 were therefore not included in this analysis as they are not expected to appear in English hospital admission records. By the start of the follow up, conditional on the patient being alive, we expected to match 3,161 English patients to the HES data set. The average age of patients at the beginning of the follow up period in this sample was 61.6 years (SD: 9.47), and 58% of the sample were males.

We found 2,985 matches to UKPDS patients in the HES records. It is important to bear in mind that it is not possible to distinguish between patients who may have never incurred a hospitalization and those who may have migrated and thus incurred costs elsewhere. Among the 2,985 matched patients, 302 were first diagnosed in centres outside England. These were dropped from the analysis as no information was available on their costs incurred outside England, or on similar patients who may have moved between countries but incurred no costs.

Additionally, of the 2,985 patients whose records were matched in the HES database, not all patients have complete information across all the fields necessary to generate HRGs, or had invalid primary diagnosis or wrong/unrecognized OPC-4 codes or ICD10 codes. This leaves us with 2,864 patients (and 27,479 records) of which 2,547 are patients first recruited in England. Out of these patients belonging to English centres, 2,398 have hospitalizations between 1997 and 2007 i.e. within the UKPDS post trial monitoring period.

Figure 1: Patients included in the study



Each hospital episode was then assigned an HRG4 (2008/2009) costing code using the HRG4 Grouper[3], which allocated that episode to one of 1,389 HRGs, organised into 54 sub-chapters, which map to 23 chapters, based on body systems[4]. In our data set 18 chapters are represented. The frequency of hospitalisations in each chapter is listed in Table 1: the most common reasons for hospitalization in our sample were related to cardiac surgery other cardiac reasons.

[3] http://www.ic.nhs.uk/casemix

[4] http://www.ic.nhs.uk/webfiles/Services/casemix/Prep%20HRG4/HRG%20v3.5%20and%20HRG4%20Comparative%20Chapter%20Analysis%202008.pdf

Table 1: Cost of HRG Chapters for the (2,383) patients in the sample

Chapter	Description	Freq.	Percent	Average Cost (£)	SD
E	Cardiac Surgery and Primary Cardiac Condition	3,614	15%	1,270	1,448
F	Digestive system	3,434	14%	1,207	1,292
L	Urinary Trans and male reproductive system	3,113	13%	1,107	1,076
D	Respiratory System	1,920	8%	1,315	1,179
H	Musculoskeletal System	1,841	8%	2,082	2,021
B	Eyes and Periorbita	1,791	7%	880	385
W	Immunology, infectious diseases and other	1,304	5%	906	853
Q	Vascular system	1,303	5%	2,503	2,415
K	Endocrine and Metabolic System	1,275	5%	1,059	806
A	Nervous System	1,075	4%	1,545	1,383
J	Skin, Breast and Burns	986	4%	1,684	1,518
S	Haematology, Chemotherapy, Radiotherapy	862	4%	834	872
G	Hepatobiliary and Pancreatic System	503	2%	1,623	1,494
C	Mouth, Head, Neck and Ears	400	2%	1,207	1,145
U	Undefined groups	345	1%	62	154
M	Female reproductive system	188	1%	1,421	887
V	Multiple trauma, emergency and urgent care	43	0%	3,268	3,056
N	Obstetrics	2	0%	562	223
	Total	23,999	100%	1,320	1,426

Table 2 shows the total number of patients incurring fatal and non fatal diabetes-related complications, conditional on the patient being alive during the follow up period. For definitions please refer to

Table A **2** in the appendix.

Table 2: Number of first event in 3,161 patients (regardless of their hospitalization status)

Event	Events occurring during:	
	1997-2007	Total time in UKPDS
MI (non fatal)	169	305
IHD (non fatal)	183	320
Stroke (non fatal)	129	190
Heart Failure (non fatal)	99	133
MI (fatal)	57	173
IHD (fatal)	43	124
CHF (fatal)	11	42
Amputation	62	80
Blindness	92	161
Cataract Ext.	457	559

Hospitalisations were then aggregated by patient year, where years are defined as 12 months intervals from the date of first diagnosis and subsequent entry into the trial. Across all follow up periods the average annual cost conditional on hospitalization was £3,348 (SD: £4,788) and the median was £ 1,790 among the 2,376 hospitalized.

Figure shows the median progression of costs both by calendar year and by diabetes duration, and Figure 2 shows the annual probability of being hospitalised.

Figure 1: HES cost per patient over time conditional on being hospitalized

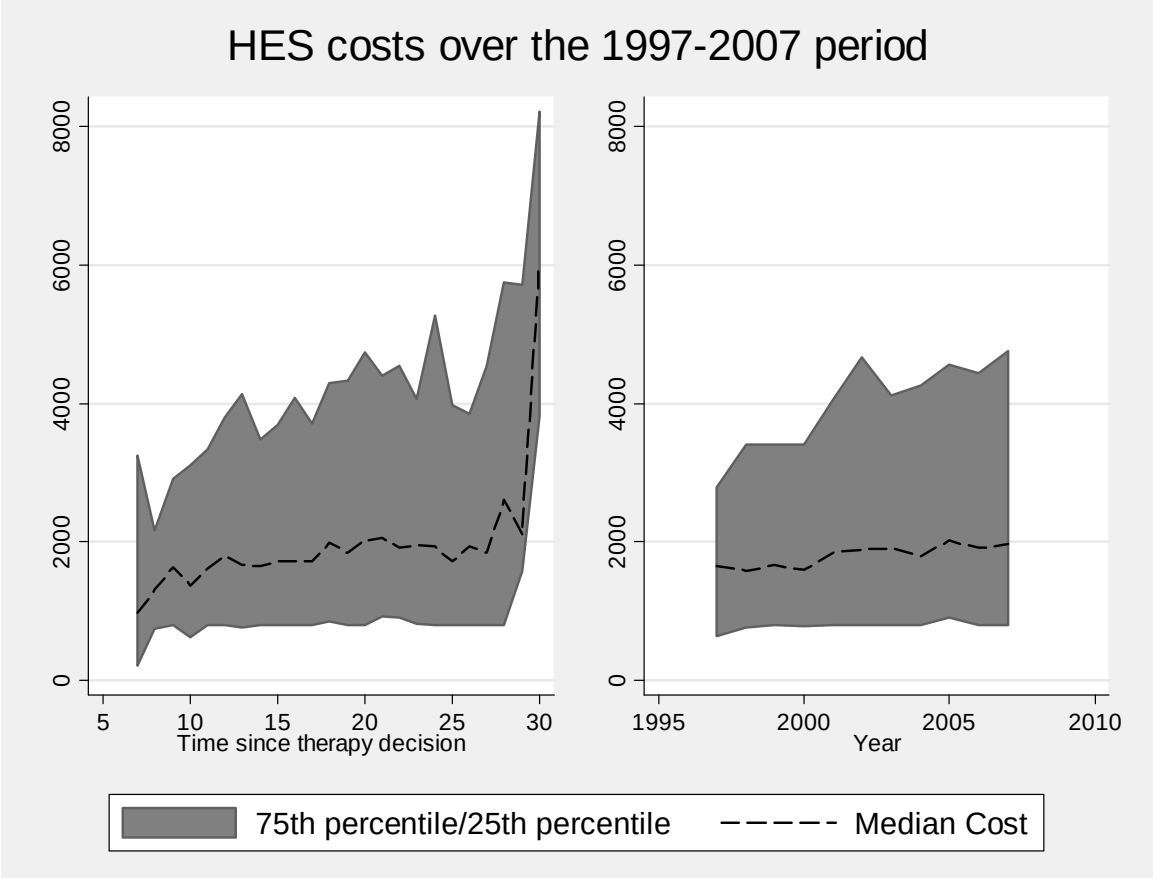
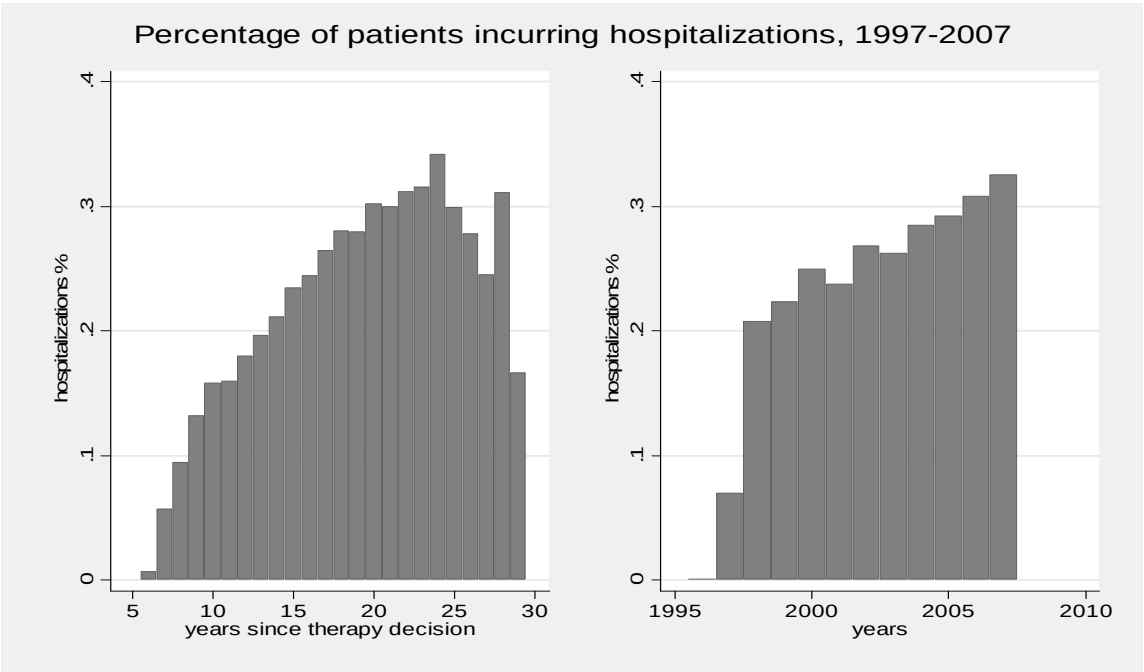


Figure 2: Probability of being hospitalized



Approximately 21.5% of patients are hospitalized in any given year. It is interesting to note that conditional on being hospitalized, the reasons for hospitalization are often apparently unrelated

to the occurrence of diabetes complications, with 87% of recorded hospitalizations occurring during years when no diabetes related complication (as defined in Table 2) occurred.

Non-inpatient care

During the UKPDS post-trial monitoring study, detailed information was collected by means of questionnaire on the use of a wide range of non-inpatient services, including all home, clinic, and telephone contacts with general practitioners, nurses, podiatrists, opticians, dieticians, and with eye and other hospital out-patient clinics. The questionnaires were administered at clinic visits or by post to patients who did not attend clinics. 7 waves of questionnaires were administered, the only difference between them being the recall period: the first questionnaire asked questions relating to use of health services over the previous *4 months*, whereas questionnaires 2 though 6 asked about utilization in the *previous year*. We annualize the information obtained in the first questionnaire. Whenever at least 1 non-empty field in the resource use questionnaire was present, all other fields were treated as zeros rather than being considered missing.

A final questionnaire (questionnaire 7), was administered to all participants in October 2007, the recall period for this was computer generated and entered into the form so as to correspond to the difference between the date of the last questionnaire sent and October 2007. The recall period thus varied between 1 month and 1 year. Where the patient was alive but had not completed the 6^{th} or earlier consecutive questionnaires, the recall period was truncated and made equal to 1 year. Given the different recall period across patients for questionnaire seven, patient's understanding of the question was examined ex-post to see if the reported resource usage was in accordance to the recall period they were given. The reported resource utilization is much higher, after anualization, than any previous questionnaire, but the average costs (and medians) do not trend upwards as the recall period increases, suggesting that most respondents did not pay attention to the changes in the wording of the question and probably assumed the recall period was 1 year as in the previous 5 questionnaires received. For this reason questionnaire 7 was not included in the analysis.

We have a total of 3495 responses for the first questionnaire and an additional 7, 425 responses from subsequent questionnaires (for a total of 10,920 complete questionnaires).

Response rates (completed questionnaires) conditional on the patient being alive varied from 71% to 76%. On average, 3 questionnaires were answered (out of 6 available questionnaires) by 3,589 patients.

The average age at the first questionnaires was 62 (SD: 9) years old. 75% of patients were English, returning 77% of all questionnaires. 16% were Scottish, returning 15% of questionnaires and 9 % of patients were from Northern Ireland, returning 8% of questionnaires (Table 3).

Table 3: Questionnaires by country

Recruiting Nations	Number of patients	Number of complete questionnaires returned
England	2693	8411
Scotland	576	1648
Northern Ireland	320	861
Total	3589	10920

The resource use data in the questionnaires were annualised where necessary, and then unit costs were attached to each item using published sources, and a resulting total annual cost was calculated. This could then be related to recorded clinical events. Table A1 in the appendix summarizes the information on unit costs, from standard national data sources, using 2009 as the reference year.

A small number of categories of non-inpatient resource utilization— GP, nurse and chiropodist visits—account for the majority of visits. The maximum number of consultations occurred amongst patients having up to two nurse visits daily.

The first questionnaire was administered in 1996/97 and the subsequent ones over the period 2002-2007. During this six-year gap resource utilization more than doubled as shown in Table 4. Part of this increase may have been driven by the publication of the UKPDS results: after the publication of trial results in September 1997, clinical guidelines were altered and practice rapidly moved towards more intensive control of blood glucose and tighter monitoring of blood pressure in hypertensive patients. This entailed a significant increase in health care utilisation. However, the observed increase between 1996/97 and 2002 onwards is also approximately in line with a more general increase in the average number of total consultations reported in the General Household Survey, where average annual consultations rose from 3.9 in 1995/1996 to 5.5 by 2008/2009.

Table 4: Annual resource utilization by type of contact and practitioner

Annual resource use	1996/7			2002-2007			
Variable	**Mean**	**Std. Dev.**	**Max**	**Mean**	**Std. Dev.**	**Max**	**P-value <0.05**
GP-Home	0.393	2.479	90	0.394	1.701	56	
GP-Surgery	**3.749**	6.03	144	**4.328**	4.801	104	*
GP-Tel	0.426	2.922	99	0.617	3.564	200	*
Nurse-Home	**1.299**	14.367	297	**4.447**	33.174	**730**	*
Nurse-Surgery	**1.736**	7.888	294	**2.866**	7.885	365	*
Nurse-Tel	0.146	2.635	132	0.372	4.5	365	*
Health Visitor-Home	0.062	0.897	36	0.134	1.669	100	*
Health Visitor-Surgery	0.021	0.336	12	0.062	1.421	104	*
Health Visitor-Tel	0.009	0.209	6	0.039	0.774	52	*
Dietician-Home	0.005	0.143	6	0.027	0.33	13	*
Dietician-Surgery	0.167	0.801	15	0.252	1.019	30	*
Dietician-Tel	0.011	0.232	9	0.036	0.433	15	*
Chiropodist-Home	0.083	0.834	27	0.409	2.473	104	*
Chiropodist-Surgery	**1.289**	2.887	48	**2.39**	5.213	135	*
Chiropodist-Tel	0.061	0.738	33	0.065	0.633	23	
Optician-Surgery	0.666	1.559	33	0.965	1.095	50	*
Optician-Tel	0.045	0.84	33	0.026	0.228	6	
Eye Clinic	0.672	1.675	27	1.17	1.706	52	*
Eye Clinic Tel	0.027	0.372	12	0.041	0.347	15	
Any other clinic	0.991	2.72	42	1.749	5.072	156	*
Any other clinic Tel	0.057	0.787	33	0.093	0.627	22	*

Table 5 reports mean total non-inpatient health care costs per patient for each questionnaire wave. We find evidence that medical expenditure increased over time and that it varies greatly across individuals, with a standard deviation which is almost 1.5 times the mean across all questionnaires. Similarly to inpatient costs, the median is considerably smaller than the average reflecting the skewness of the data, which has implications for the modelling strategy to be used.

Table 5: Total Annual cost (£)

Costs	Q1	Q2	Q3	Q4	Q5	Q6	Total
Mean	424	670	677	663	728	711	603
Std. Dev.	718	1108	1029	1014	1266	1036	997
Median	219	413	418	424	420	441	366
Skewness	6.9	8.2	7.6	8.8	7.5	5.4	7.9

Given that questionnaire one had a different recall period than the subsequent questionnaires used and that, even after annualisation, the mean was considerable lower than the questionnaires administered six or more years later, it is worth asking whether it makes sense to include the first questionnaire for analysis. However, as Figure 3 shows, the relative effect of having

a complication compared with not having one appears to be similar across the first and subsequent questionnaire waves, suggesting that, once properly accounted for by the use of an indicator, the first questionnaire can be safely analysed together with the others.

Figure 3: Total costs with and without complications per questionnaire round

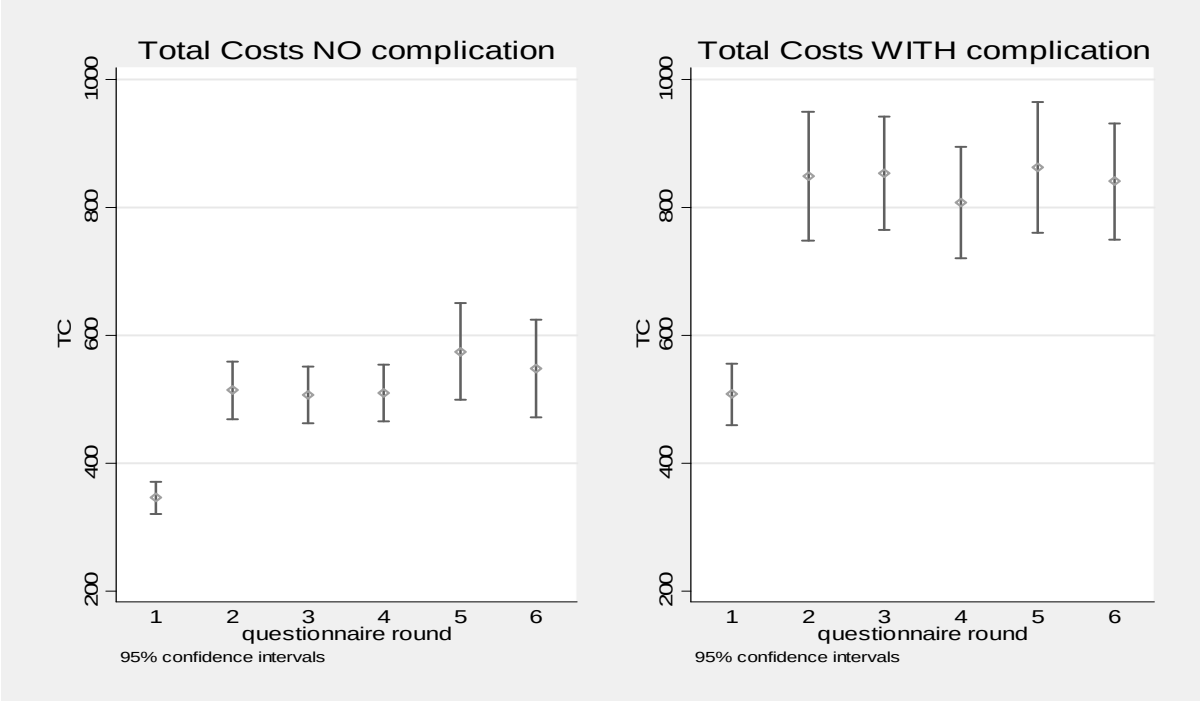


Table shows the total number of events incurred in patients answering at least one resource use questionnaire and the number of patients experiencing them. Amputations and eye treatments are more likely to reoccur than any other complication. Table 6 differs from Table 2 in that the sample under consideration is different (the former refers to 3161 English patients only while the latter refers to the 3589 patients completing a questionnaire, including England, Scotland and Northern Ireland). The last column of both tables are however comparable as they provide the total number of patients experiencing at least one event since diagnosis.

Table 6: Total number of events and number of responders experiencing them

Non Fatal Events	Number of events	Patients with events
MI	451	384
IHD	435	428
Stroke	275	246
Amputation	163	108
Blindness to 1 eye	248	227
Heart Failure	196	193
Cataract Extraction	1066	712

Finally, before considering the estimation models, it is worth noting that patients who report never using non-inpatient services do nevertheless have complications, while those with no recorded diabetes-related complications do nevertheless make use of non-inpatient services. As Table 7 shows, approximately 21% (55/259) of those who never reported a cost have complications, while (similarly to inpatient care), 90% of those using non-inpatient services do not report any diabetes-related complication.

Table 7: Patients' complications and costs

Matrix	TC=0	TC>0	**Total**
No Complication	204	1,784	1,988
Complication	55	1,546	1,601
Total	259	3,330	**3,589**

3- Model

As a broad modelling strategy, for both inpatient and non-inpatient resource use, we employ a two-part model. This is because we are interested in the unconditional expenditure equation, describing the costs incurred by all patients, including non-utilisers.

In the first part, a logistic regression is used to model the probability of incurring some costs within a single patient-year time period. The dependent variable is set equal to 1 in any patient year (or patient questionnaire, in the case of non-inpatient resource use) an individual incurs costs. In the second part the total costs incurred are estimated, conditional on incurring any costs. As the events amputation and cataract extraction are treatments requiring hospitalization, we constrain the coefficients on these variables in the first-stage equation (i.e. the probability of attending hospital is set equal to 1).

Part 1:

Random Effect Logit : $\Pr(C_{it} > 0 | X_{it}^{j}) = \frac{\exp(\alpha^{j} X_{it}^{j})}{1+\exp\left(\alpha^{j} X_{it}^{j}\right)}$

Where X is the vector of covariates of interest, α indicates the estimated coefficient for the j^{th} variable of interest and the subscripts *i* and *t* indicate the patient and the time period respectively.

In the second stage of the two part model, to address the skewness and heavy right tails present in the data, we use the panel version of a generalized linear model (GLM), with a mean function (between the linear predictor and the mean) and a variance function (between the mean

and variance on the original scale). This approach addresses linearity in response on the specified scale and accommodates skewness through variance weighting (Mihaylova et al., 2010).

In order to specify the relationship between the set of regressors and the conditional mean we test for two link functions: the identity link and the log link (see Appendix). The former has the benefit of ease of interpretation, as the coefficients read in the same way as OLS irrespective of the choice of distribution. In the latter, covariates act multiplicatively on the mean, changing the interpretation of the coefficients ($E[y|x]=\exp(x'\beta)$ and thus $\ln(E[y|x])=x'\beta$).

We use the gamma distribution, as costs are constrained to be positive, in order to describe the relationship between variance and conditional mean. This places less weight on outliers (ie patients with high costs) than the normal distribution.

$$var[y|x] = (E[y|x])^2$$

Ultimately, however, we are interested in the impact of complications on costs in terms of levels. In the case of a GLM model, no retransformation is needed: the expected unconditional cost is the product of the expectation of estimates from parts 1 and 2. In order to obtain a measure of uncertainty for these estimates, we calculate 95% CIs for estimates of the cost for complications through non-parametric bootstrapping. This is done by randomly re-sampling individuals with replacement and re-estimating the equations. Costs are then calculated and rank-ordered, and the 2.5th and 97.5th estimates are taken as the confidence limits.

Part 2

Model 1: GEE identity link, gamma distribution: $E(C_{it}|C_{it} > 0, X_{it}) = \beta^j X_{it}^j,\ var[y|x] = (E[y|x])^2$

Model 2: GEE log identity link, gamma distribution: $E(C_{it}|C_{it} > 0, X_{it}) = \exp(\beta^j X_{it}^j),\ var[y|x] = (E[y|x])^2$

4- Results

Inpatient

Table reports the coefficients and standard errors for the two-part model that can be used to predict hospital in-patient costs. The log linked gamma represents the log-rate of the response, the specification is thus identical to exponential regression. Because the model uses the long link, we can interpret the exponentiated coefficients as multiplicative effects on expected costs. Thus for example, having a non fatal myocardial infarction (MI) multiplies the estimated costs by exp(0.590)=1.80, equivalent to an 80% increase.

In order to ascertain the appropriate link function to be used we regress total costs on the prediction and the prediction squared. If a model with identity link is specified correctly the prediction squared would have no explanatory power. We find that that is not the case, suggesting that the use a log link would be a more appropriate choice.

Table 8: Regression equations to derive annual probability of incurring hospital costs, and costs of hospital care conditional on incurring a cost

Part 1: Equation to derive annual probability of incurring hospital costs			**Part 2: Equation to derive annual cost of hospital care, conditional on costs being incurred**		
RE Logit			**GEE Gamma distribution log link**		
Variable	*Coefficient*	*SE*	*Coefficient*	*SE*	*Multiplicative effect*
Constant	-2.235**	(0.053)	7.878**	(0.034)	
Current age – 60 (years)	0.069**	(0.003)	0.012**	(0.002)	1.01
Male (=1)	0.024	(0.057)	0.050	(0.038)	1.05
Event during year indicator		0.316		-0.014	
Fatal MI	0.316	(0.198)	-0.014	(0.133)	0.99
Fatal IHD	0.054	(0.236)	-0.076	(0.198)	0.93
Fatal CHF	-0.560	(0.406)	0.307	(0.216)	1.36
Non-fatal MI	1.924**	(0.189)	0.590**	(0.090)	1.80
Non-fatal IHD	2.210**	(0.189)	0.690**	(0.090)	1.99
Non-fatal stroke	1.359**	(0.215)	0.501**	(0.112)	1.65
Heart failure	1.619**	(0.252)	0.435**	(0.117)	1.54
Amputation	1.000	(0.000)	1.028**	(0.151)	2.80
Blindness in one eye	0.490	(0.262)	-0.058	(0.211)	0.95
Cataract extraction	1.000	(0.000)	-0.404**	(0.061)	0.67
History of event†		0.473**		0.035	
Non-fatal MI	0.473**	(0.092)	0.035	(0.055)	1.04
Non-fatal IHD	0.574**	(0.089)	0.134*	(0.059)	1.14
Non-fatal stroke	0.413**	(0.117)	0.148*	(0.060)	1.16
Heart failure	0.942**	(0.137)	0.260**	(0.078)	1.30
Amputation	0.436*	(0.186)	1.025**	(0.158)	2.79
Blindness in one eye	0.461**	(0.125)	-0.001	(0.079)	1.00
Cataract extraction	0.195**	(0.068)	0.004	(0.050)	1.00
Observations	33131		7239		
Number of patients	3161		2376		

†Refers to events that occurred in previous patient years.

** p<0.01, * p<0.05

Table 9: Estimated probability of incurring some hospital in-patient costs, estimated annual hospital in-patient costs conditional on cost being incurred, for a representative individual by first diabetes-related complication, during year of complication and in subsequent years

	probability of incurring some hospital in-patient costs		Estimated annual hospital in-patient costs conditional on cost being incurred (GEE Gamma Model with Link Function)		Expected hospital in-patient cost of complication	
Event	Mean	95% CI	Mean (£)	95% CI	Mean (£)	95% CI
No Complication	0.14	(0.13, 0.15)	2,941	(2,768, 3,126)	412	(360, 430)
Event during year indicator						
Fatal MI	0.18	(0.12, 0.23)	2,899	(2,222, 3,783)	522	(312, 742)
Fatal IHD	0.14	(0.09, 0.20)	2,726	(1,850, 4,017)	382	(212, 616)
Fatal CHF	0.08	(0.02, 0.14)	3,997	(2,611, 6,120)	320	(86, 711)
Non-fatal MI	0.52	(0.43, 0.62)	5,305	(4,451, 6,323)	2,759	(1927, 3534)
Non-fatal IHD	0.59	(0.50, 0.68)	5,864	(4,907, 7,007)	3,460	(2631, 4101)
Non-fatal stroke	0.38	(0.28, 0.48)	4,854	(3,904, 6,035)	1,845	(1222, 2552)
Heart failure	0.44	(0.32, 0.57)	4,545	(3,597, 5,741)	2,000	(1330, 2852)
Amputation	1		8,222	(6,105, 11,074)	8,222	(6799, 10146)
Blindness in one eye	0.23	(0.14, 0.32)	2,776	(1,834, 4,202)	638	(297, 924)
Cataract extraction	1		1,963	(1,738, 2,218)	1,963	(1500, 2681)
History of event						
Non-fatal MI	0.21	(0.18, 0.24)	3,045	(2,747, 3,375)	639	(478, 731)
Non-fatal IHD	0.22	(0.19, 0.25)	3,362	(2,984, 3,787)	740	(573, 901)
Non-fatal stroke	0.19	(0.16, 0.23)	3,409	(3,026, 3,841)	648	(498, 829)
Heart failure	0.29	(0.24, 0.35)	3,816	(3,258, 4,471)	1,107	(739, 1433)
Amputation	0.18	(0.12, 0.23)	8,201	(5,980, 11,246)	1,476	(902, 2691)
Blindness in one eye	0.21	(0.17, 0.26)	2,939	(2,504, 3,449)	617	(423, 779)
Cataract extraction	0.14	(0.12, 0.16)	2,954	(2,654, 3,287)	414	(396, 562)

In order to report results in levels, we need to resort to a representative patient. Table 9 reports predictions from the logistic regression and generalized estimating equation with gamma distribution, for an individual with characteristics set to reflect the average values for the UKPDS study population at follow up (i.e. a male aged 65 years) for the first complication of any type.

From the first column of Table 9 we can see that patients who had no complications had a probability of incurring any hospital in-patient costs in any single year of 0.14 (much higher than the comparable 0.06 found in Clarke et al (2003) using the first 20 years of clinical records); that is, approximately 14% of patients who did not have any diabetes related complications in a given year nevertheless were admitted to hospital as an in-patient and consequently incurred some hospital costs. Table also reports the annual probability of incurring any hospital costs for each type of event in the same year as the hospitalization as well as in any previous years. The immediate impact of complications such as a MI is to increase the marginal probability of incurring some hospital in-patient costs (e.g. a 52% probability). Thus approximately half of all non-fatal MIs do not incur any hospital in-patient costs in the year in which they occur, and this may be due to patients not being diagnosed as having had an MI until a subsequent investigation. Patients with a history of

complications also appear to have a higher probability of hospitalizations compared to those who have not experienced prior complications.

The second column of Table 9 shows the estimated mean hospital inpatient costs associated with each complication conditional on the patient being hospitalized. Thus, if the patient incurred hospital in-patient costs in the year in which they had a non-fatal MI, these costs averaged £5,305 (4,451, 6,323), while patients who experienced an amputation on average incurred hospital in-patient costs of £8,222 (6,105, 11,074) in that year. For all complications except fatal MI, fatal IHD and cataract extraction, these hospital in-patient costs are substantially higher than the £2,941 incurred average by the 14% of patients with no complication who nevertheless were admitted to hospital as in-patients.

The last column of Table 9 shows the product of the previous two columns, i.e. the expected hospital in-patient costs associated with each complication. For example, someone who experiences a non-fatal stroke has a 38% probability of incurring hospital in-patient costs in the year the event occurred, the cost for these 38% of patients was £4,854 (£3,597, £5,741) and so the expected or unconditional hospital in-patient costs associated with a non-fatal stroke are the product of these, or £1,845 (£1222, £2552). Note that the 95% confidence intervals around these estimates are not symmetrical, due to the effects of retransformation.

Non-inpatient

Results for the two-part model for non-inpatient costs are shown in Table 10. As controls we use the demeaned current age, gender, an indicator equal to 1 if the questionnaire is any other than the first one and an indicator for whether the patient was first recruited in and English centre or not (to make results comparable with the hospitalizations records collected for English patients only). 7.2% of questionnaires report no contact with healthcare providers and so incur no costs. This varies greatly between the first and subsequent rounds. We cluster standard errors at the patient level and perform a Wald test on the coefficients of the short and long run being the same. While one cannot reject the hypothesis that the coefficients are equal to each other in the first part equation (chi2(7)= 7.10, Prob > chi2 = 0.4186) – that is, the probability of incurring a cost is not greatly different if the complication has occurred in the period of the recall or in previous periods – it does appear that in part 2 the coefficients of short term and long term are statistically different (chi2(7) = 17.76, Prob > chi2 = 0.0131). The marginal impact of complications on non-inpatient costs is statistically significant for all the clinical endpoints.

Table 10: Regression equations to derive annual probability of incurring outpatient costs, and costs of outpatient care conditional on contacts

Part 1: Equation to derive annual probability of incurring outpatient costs			**Part 2: Equation to derive annual cost of outpatient care, conditional on costs being incurred**		
	RE Logit		**GEE Gamma distribution log link**		
Variable	*Coefficient*	*SE*	*Coefficient*	SE	*Multiplicative effect*
Constant	2.192**	(0.163)	6.326**	(0.050)	
Current age – 60 (years)	0.023**	(0.005)	0.010**	(0.003)	1.01
Male (=1)	-0.636**	(0.104)	-0.222**	(0.043)	0.80
England (=1)	-0.002	(0.112)	-0.084	(0.049)	0.92
Questionnaire number >1	3.075**	(0.157)	0.234**	(0.043)	1.26
Event during year indicator					
Non-fatal MI	1.788	(1.070)	0.538**	(0.081)	1.71
Non-fatal IHD	20.368	(11,072.119)	0.310**	(0.085)	1.36
Non-fatal stroke	-0.020	(0.845)	0.537**	(0.124)	1.71
Heart failure	20.016	(16,448.917)	0.373**	(0.129)	1.45
Amputation	-1.615	(0.865)	0.926**	(0.172)	2.52
Blindness in one eye	0.291	(1.128)	0.573*	(0.292)	1.77
Cataract extraction	1.158	(0.647)	0.138**	(0.053)	1.15
History of event†					
Non-fatal MI	0.494*	(0.232)	0.186**	(0.056)	1.20
Non-fatal IHD	0.303	(0.221)	0.166**	(0.061)	1.18
Non-fatal stroke	0.060	(0.339)	0.323**	(0.094)	1.38
Heart failure	0.949	(0.563)	0.462**	(0.090)	1.59
Amputation	0.515	(0.693)	0.907**	(0.147)	2.48
Blindness in one eye	0.480	(0.337)	0.279*	(0.124)	1.32
Cataract extraction	-0.019	(0.227)	0.180*	(0.070)	1.20
Observations	10920		10238		
Number of patients	3589		3330		

†Refers to events that occurred in previous patient years.
** p<0.01, * p<0.05

In Table 11 we predict costs for a representative individual: an English Male, 65 year of age and answering more than one questionnaire and therefore in the period following the 1997 dissemination of UKPDS findings (by the time the second questionnaire was administered (2002), changes in the protocol for the management of disease were already in place). As before, the 95% CI for the costs estimates in Table 11 were obtained through non-parametric bootstrapping involving 1000 replications and obtained by randomly re-sampling individuals with replacement and re-estimating the equations.

Post 1998, even for patients with no complications, the probability of incurring some non-inpatient costs in any year is virtually 100%. Similarly to inpatient care, amputations are the most costly diabetes complication in the non-inpatient setting.

Table 11: Estimated probability of incurring out-patient costs, estimated annual outpatient costs conditional on cost being incurred, for a representative individual by first diabetes-related complication, during year of complication and in subsequent years

	Probability of incurring some out-patient costs		Estimated annual out-patient costs (GEE Gamma Model with Link Function) conditional on cost being incurred		Expected out-patient cost of complication	
Event	Mean	95% CI	Mean (£)	95% CI	Mean (£)	95% CI
No Complication	0.991	(0.988, 0.995)	546	(510, 584)	541	(419, 595)
Event during year indicator						
Non-fatal MI	0.999	(0.995, 1)	934	(789, 1106)	933	(767, 1106)
Non-fatal IHD	1		744	(627, 884)	744	(592, 860)
Non-fatal stroke	0.991	(0.976, 1)	934	(730, 1195)	926	(792, 1203)
Heart failure	1		792	(614, 1022)	792	(631, 969)
Amputation	0.958	(0.889, 1)	1,378	(981, 1935)	1,320	(1001, 1535)
Blindness in one eye	0.994	(0.979, 1)	968	(544, 1722)	962	(735, 1476)
Cataract extraction	0.997	(0.994, 1)	627	(560, 702)	625	(545, 723)
History of event						
Non-fatal MI	0.995	(0.992, 0.998)	657	(589, 733)	654	(579, 765)
Non-fatal IHD	0.994	(0.990, 0.997)	644	(571, 726)	640	(563, 722)
Non-fatal stroke	0.992	(0.986, 0.998)	754	(628, 905)	748	(599, 907)
Heart failure	0.997	(0.993, 1)	866	(724, 1037)	863	(703, 1008)
Amputation	0.995	(0.988, 1)	1,352	(1009, 1811)	1,345	(876, 1576)
Blindness in one eye	0.995	(0.990, 0.999)	721	(561, 928)	718	(545, 830)
Cataract extraction	0.991	(0.986, 0.996)	653	(560, 762)	647	(575, 715)

5- Discussion

These results provide estimates of the immediate and long-term healthcare costs associated with seven major diabetes-related complications.

Relatively few studies have analyzed the impact of complications on health care costs using patient-level data, and the majority of these are US-based (O'Brien, Shomphe et al. 1998). In the UK most studies are based on population prevalence using a bottom-up approach (Dixon, Currie et al. 2000). Clarke et al. (2003) provide one UK exception: their estimates of resource use are based on a cross-sectional study of patients enrolled in the UKPDS who had answered the first 1996/7 questionnaires, and their results have been widely used. However, that paper had to group complications into micro and macro-vascular events when analysing non-inpatient costs because there was not enough power from a single survey to distinguish each type of diabetes-related complications.

Our results indicate the substantial impact of many diabetes related complications on hospital costs, not only in the year in which the event occurs, but in permanently raising the average level of hospital costs in all subsequent years. This effect could not easily be observed in the absence of patient-specific data, and may arise because patients carrying a history of diabetes-related

complications become more expensive and difficult to treat for other health care problems when they occur.

The costs of non-inpatient care have been relatively neglected in previous studies, perhaps being perceived as less important than inpatient care. Approximately 80% of conditional costs are in fact accounted by hospitalizations; yet there is not much difference in terms of unconditional costs, even in the absence of complications for an elderly diabetic population between inpatient and non-inpatient costs.

This work suggests at least three avenues for further research. First, the work could be extended further to include pharmaceutical and related (needles, test strips etc) expenditures. Second, the scope of the work could be extended to estimate the impact of diabetes and diabetes-related complications on non-health care costs including social care, long term care and patient incurred and societal costs. Third, the types of complications considered could be extended beyond the seven diabetes-related complications included here (non-fatal MI, non-fatal IHD, non-fatal stroke, heart failure, amputation, blindness in one eye, cataract extraction) to include fatal events, and other events such as renal disease or failure and foot ulcers.

Appendix

Table A 1: **Unit costs of non-inpatient health services**

	Seen at home	Surgery visit	Telephone advice	Source
General Practitioner (exc. Drugs)	£4.50 per minute or **£105** per home visit lasting 23.4 minutes (includes travel time of 12 min)	**£31** per consultation lasting 11.7 minutes	**£19** for 7.1 minutes	Lesley Curtis PRSSU 2009. Table 8.8b, page 121
Nurse	**£20** per home visit including qualifications and travel	**£11** per consultation	6 min. £43 per hour. **£4.3**	Lesley Curtis PRSSU 2009. Table 8.6, page 118. For telephone time: table 8.7
Health visitor	**£41** per home visit (20 minutes)	£82 per hour of clinic contact. Assume 15 min. **£20.5**	£34 per hour. Assume 6 min. **£8.2**	Lesley Curtis PRSSU 2009. Table 8.3, page 115
Dietician	£60 per hour of home visiting + £2.70 per travel visit. Assume 25 min. **£27.70**	£33 per hour in clinic Assume 20 min. **£11**	£35 per hour of client contact Assume 10 min. **£5.83.**	Lesley Curtis PRSSU 2009. Table 11.4, page 150
Chiropodist	£21 per home visit; £1.40 per travel time visit. **£22.40**	**£11** per clinic visit	Assume 10 min. at £23 per hour contact time. **£3.83**	Lesley Curtis PRSSU 2009. Table 7.4, page 108
Optician		Sight-test fees **£18.39p** agreed for 2005-06. Adjusted HSHC pay & price: £**21.14**	**£4.3** (estimated to be the same as nurse)	Department of Health: review body on doctors' and dentists' remuneration 2004.
Hospital eye clinic		**£62.39.** Adjusted HSHC pay & price: £**74.10**	**£4.3**	Average cost per out-patient ophthalmology consultation, England 2004, TFR2 return.
Any other hospital clinic		**£128** Average cost of a consultant-led first attendance non-admitted face to face	**£4.3**	NHS Reference Costs 2008/09, tables TEI, TNEI_S and TNEI_L.

Table A 2: **Diabetes-related complications included in the regression analysis, with diagnostic definitions**

Event	Predefined diagnostic definitions
MI (non fatal)	ICD9 Code 410
IHD (non fatal)	ICD9 Code 411 to 414.9
Stroke (non fatal)	Major stroke with symptoms that persist more than 1 month (ICD9 Codes 430 to 434.9 and 436)
Heart Failure (non fatal)	ICD9 Codes 428 to 428.1
MI (fatal)	ICD9 Codes 410 to 411; ICD9 Codes 798 to799
IHD (fatal)	ICD9 Code 411 to 414.9
CHF (fatal)	ICD9 Code 428 to 428.9
Amputation	Major limb complications requiring amputation of digit or limb for any reason (ICD9 Codes 5.845 to 5.848)
Blindness	ICD9 Code 369 to 369.9
Cataract Extraction	ICD9 Codes 5.143 to 5.146

***Link test** (Ref. McCullagh, P. and J.A. Nelder. 1989. Generalized Linear Models. Chapman and Hall: London)

```
xtgee tot_cost age_cent  male  $events_65 $history_65 if costind>0, family(gaussian) link(identity)
predict yhat_forl if e(sample)
gen yhat_forlsq=yhat_forl^2
reg tot_cost yhat_forl  yhat_forlsq
```

```
. reg tot_cost yhat_forl  yhat_forlsq

      Source |       SS       df       MS              Number of obs =    7239
-------------+------------------------------           F(  2,  7236) =  227.20
       Model |  9.8024e+09     2  4.9012e+09           Prob > F      =  0.0000
    Residual |  1.5610e+11  7236  21572418.7           R-squared     =  0.0591
-------------+------------------------------           Adj R-squared =  0.0588
       Total |  1.6590e+11  7238  22920759.4           Root MSE      =  4644.6

------------------------------------------------------------------------------
    tot_cost |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   yhat_forl |   .2654427    .170489     1.56   0.120    -.0687655    .5996509
  yhat_forlsq |   .0000577    .000015     3.85   0.000     .0000283    .0000872
       _cons |   1758.223   386.6659     4.55   0.000     1000.245    2516.201
------------------------------------------------------------------------------
```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