Steps towards cost-benefit analysis of regional neurosurgical care

J D Pickard, S Bailey, H Sanderson, M Rees, J S Garfield

Abstract

***Objective*—To determine the cost of averting death or severe disability by neurosurgical intervention.**

***Design*—Retrospective analysis of one year's admissions for neurosurgery; comparison of outcome with expected outcome in the absence of neurosurgical intervention and with the cost of neurosurgery.**

***Setting*—Wessex Neurological Centre.**

***Patients*—1026 Patients were admitted to the neurosurgical service in 1984. Of 1185 admissions, 978 case records were available and outcome was known in 919.**

***Main outcome measures*—Outcome was assessed with the Glasgow outcome scale, modified as necessary, from the case notes, or by letter follow up to the general practitioner. Expected outcomes for each of the 54 diagnoses were derived from both published reports where available and an expert panel of 18 consultant neurosurgeons. The cost of the neurosurgical service for 1983-4 was known from a separate study and the cost per patient was calculated using the length of stay.**

***Results*—The cost of neurosurgery in 1983-4 was £1·8 million. In all, 243 deaths or severe disabilities were estimated to have been averted at an average cost of £7325 (range £5000 to £70 000). The overall cost per quality adjusted life year (QALY) was £350 (range £34 to >£400 000). The cost of long term care for severely disabled survivors is at least 18-fold greater than the cost of neurosurgical intervention to avert such disability.**

***Conclusions*—In Britain neurosurgery is not expensive in comparison with the costs and benefits of other areas of medicine, and the cost per QALY is unexpectedly low except for severe diffuse head injury, malignant brain tumours, and cerebral metastases. The neurosurgical budget should be assessed in the context of managing a patient in hospital and subsequently in the community.**

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Introduction

The costs of running a regional neurosurgical unit, and how these costs should be controlled and related to outcome, are matters that have engaged neurosurgeons, health service planners, and managers for some time.[1-7] They have been made more urgent by recent changes in legislation. The opportunity for a comprehensive cost-benefit analysis of regional neurosurgical care arose when the Wessex Regional Health Authority and the Southampton and South West District Health Authority funded the detailed costing of the Wessex regional neurological and cardiothoracic units for the year 1983-4.[8]

We defined the "product of care" and the cost for each major neurosurgical diagnostic group by considering outcomes and costs of inpatient care, mainly in relation to life expectancies and the natural course of the diseases.

Diagnostic categories and groups

"Subarachnoid haemorrhage"—aneurysm, arteriovenous malformation, spontaneous haematoma, unruptured aneurysms, unexplained subarachnoid haemorrhage, suspected but unconfirmed subarachnoid haemorrhage

Head injury—extradural haematoma, intradural haematoma, chronic subdural haematoma, compound depressed fracture, cerebrospinal fluid rhinorrhoea, diffuse and unspecified head injuries

Intracranial tumours—glioma (high grade or low grade), oligodendroglioma, haemangioblastoma, ependymoma, medulloblastoma, acoustic neuroma, craniopharyngioma, meningioma, pituitary (non-functioning; prolactinomas, those causing acromegaly, Cushing's syndrome, apoplexy), miscellaneous

Spinal disorders (non-metastatic)—congenital, prolapsed lumbar intervertebral disc, lumbar spondylosis, cervical spondylotic myelopathy, cervical spondylotic radiculopathy, spinal abscess, neurofibroma, meningioma, angioma, ependymoma, glioma, miscellaneous spinal disorders

Central nervous system metastases—intracranial, spinal

Miscellaneous—cerebral abscess, encephalitis, meningitis, acute hydrocephalus, normal pressure hydrocephalus, benign intracranial hypertension, epilepsy, trigeminal neuralgia, carpal tunnel syndrome, non-haemorrhagic cerebrovascular disorders, miscellaneous and unclassified disorders

Methods

The Wessex Neurological Centre provides a neurosurgical service for a population of 2·7 million (1984). Outcomes of neurosurgical care for patients discharged during 1984 were assessed six months or more after discharge. During this year there were 1185 admissions of 1026 patients. Of the 978 patients with available case records, 919 (94%) were followed up and assessed. Fifty four diagnostic categories were defined, including a "miscellaneous/undiagnosed" category, and these were classified in six broad groups (above box). Final diagnosis, age, sex, and total length of inpatient stay were obtained from the case records.

OBSERVED OUTCOMES

Information was based on the case notes or follow up letters sent to the general practitioners. Patients were graded using the Glasgow outcome scale,[9] which ranges from 1 (death) to 5 (no disability) (box). This scale is rather crude but it has been thoroughly tested for reliability and validity.[10] It was modified where necessary—for example, for patients with pituitary

tumours (associated with visual or endocrine pathology) or spinal problems (associated with pain or problems of mobility and power). Patients with degenerative spinal disorders whose condition remained the same after operation were graded 3 (severe disability) even when the realistic aim of surgery was to prevent further deterioration and not necessarily to facilitate improvement.

EXPECTED OUTCOMES WITHOUT NEUROSURGERY

In each diagnostic category an estimate of the likely outcome at six months and after 10-20 years in the absence of neurosurgical intervention was derived from published data or from a written questionnaire completed independently by a panel of 18 consultant neurosurgeons from throughout the United Kingdom (unpublished data). The spectrum of severity of the disorder was defined as that to be expected on presentation to a typical British regional neurosurgical unit. The population with subarachnoid haemorrhage was particularly well defined because of a concurrent prospective double blind randomised trial.

CALCULATION OF COSTS AND THE PRODUCT OF CARE

The cost of neurosurgery for the year 1983-4, extracted from Rees's report,[8] was £1 795 000. Information about admissions and lengths of stay came from two overlapping sets of data, the neurological centre's own records of admission, and the SH3 statistics (aggregated statistics of bed use before 1987 based on bed occupancy at midnight in each ward). The SH3 data are likely to be the more complete but do not relate to individual patients and could therefore be used only to estimate an average cost of bed days. Thus the SH3 data were used to determine the total bed days for the year (12 318) and hence the cost per occupied bed day. No attempt was made retrospectively to define nurse dependency or costs for investigation or operating theatre by diagnostic group.

DEFINITION OF "PRODUCT OF CARE"

The "product of care" was defined as the number of patients in whom severe disability or death was expected but averted by neurosurgery:

Product of care = expected minus observed bad outcomes, where bad outcomes are deaths, persistent vegetative states, and severe disabilities;

Expected bad outcomes = percentage of predicted bad outcomes × (n − NFU), where n is the number of patients per diagnostic group and NFU is the number of patients not followed up. The cost of averting a bad outcome is therefore the total cost of care for each diagnostic group divided by the product of care. Life expectancy for each diagnosis was calculated from the age and sex distribution (life tables for England and Wales, Government Actuary's department). Correction was applied for various conditions: (*a*) malignant tumours and metastases, by longer follow up, and using panel data and published data[11]; (*b*) subarachnoid haemorrhage of unknown cause, using data of Hawkins *et al*[12]; (*c*) severe disability after head injury, using data of Walker *et al*[13]; and (*d*) paraplegia and tetraplegia, using data of Geisler *et al*.[14]

Grading the outcome of neurosurgery

Glasgow outcome scale	*Appropriate modification*
1 Death	Death
2 Vegetative	Deterioration
3 Severe disability (dependent)	No improvement but no deterioration
4 Moderate disability (independent)	Some improvement
5 No disability (good recovery)	Pain free; fully mobile; normal vision, etc

Acceptable life years (aLY) were defined as (product of care) × (adjusted life expectancy). Acceptable life years saved refers to the number of deaths, persistent vegetative states, and severe disabilities averted. An estimate of the cost per acceptable life year saved for each diagnosis was then calculated as:

Cost per aLY = cost of averting bad outcome ÷ aLY saved. This cost per acceptable life year was then modified to take account of the patients who did not make a good recovery but remained moderately disabled:

Cost per QALY = cost of averting bad outcome ÷ (aLY saved × F), where QALY is a quality adjusted life year[15,16] and F is the adjustment for the proportion of patients left with a moderate disability:

$F = 1 - (MD \div (MD + GR))(1 - V)$, where MD is the number of moderate disabilities, GR is the number of good recoveries, and V is the value accorded to each life year saved with a moderate disability (V = 0·5 on a scale 0-1, where good recovery scores 1 and death or severe disability scores 0). The cost of survival with a severe disability was examined separately. The probable ranges of values for the product of care for each diagnostic group for which detailed published studies were not available are shown in the appendix, tables A1-A6.

Results

COSTINGS

From costs given by Rees[8] and SH3 data for total occupied bed days in 1984, a cost per patient day of £146 was calculated. The mean length of stay for patients in each diagnostic category was calculated from examining individual case notes. Complete hospital activity analysis data were not available for 1984.

COSTS OF AVERTING DEATH OR SEVERE DISABILITY

For each diagnostic category the total cost was calculated from the length of stay multiplied by £146, and the cost of averting a death or severe disability was derived by dividing the total cost by the difference

TABLE I—*Summary of cost of averting bad outcome by neurosurgical intervention and cost per QALY*

Diagnosis	No of patients	Total length of stay (days)	Total cost (£)	Bad outcomes averted	Cost per bad outcome averted (£)	Mean (range) of cost per aLY (£)*	Mean (range) of cost per QALY (£)*
Subarachnoid haemorrhage	178	2 237	326 602	45	7 258	279 (173-∞)	310 (192-∞)
Head injury	161	1 317	192 282	35	5 494	137 (37-∞)	151 (41-∞)
Intracranial tumours:							
Malignant	116	1 876	273 896	4	68 474	61 138 (788-332 008)	68 694 (788-400 010)
Benign	82	1 489	217 394	39	5 574	199 (135-394)	243 (148-588)
Spinal disorders (non-metastatic)	159	2 286	333 756	64	5 215	193 (57-343)	261 (76-476)
CNS metastases	66	610	89 060	8	11 133	11 133	
Miscellaneous	216	2 376	346 896	48	7 227	241 (34-3 260)	307 (34-4 180)
Total (range)	978†	12 191	1 779 886	243	7 325	293 (34-∞)‡	351 (34-∞)

*Ranges refer to different diagnoses within major diagnostic group; aLY = acceptable life year saved, QALY = quality adjusted life year.
†48 Case records were not available and hence 127 occupied bed days (12 318−12 191) are unaccounted for. Outcomes were known in 919 patients.
‡Overall mean life expectancy = 25 years.

TABLE II—*Cost of averting severe disability (SD) and persistent vegetative state (PVS) excluding death*

Diagnosis	No of patients	Bad outcomes: Observed (at 6 months)	Bad outcomes: SD or PVS expected	Expected minus observed	Cost of neurosurgical intervention (£)	Cost per SD or PVS averted (£)	Standard life expectancy	Corrected life expectancy*	Projected working life	Cost per patient of long term care (excluding loss of earnings (£)†	Total cost of long term care averted (£m)
Subarachnoid haemorrhage‡	178	3	15‡	12	326 602	27 217	31	26	15	474 500	5·7
Acute head injury	145	8	13·3§	5·3	158 118	29 834	43	38	33	693 500	3·67
Chronic subdural haematoma	16		4·5§	4·5	34 164	7 592	11	6		109 500	0·49
Cerebral abscess	11		1§	1	38 398	38 398	31	26	18	474 500	0·47
Total	350			22·8	557 282						10·33

*Corrected according to Walker *et al*[11] (crude estimate).
†Cost of care in an institution or at home is £50-£70 a day plus social security payments—assume £18 250 a year at £50 a day.
‡Expected severe morbidity at 20 years based on Winn *et al*[17] for aneurysms and Pool[18] and Crawford *et al*[19] for arteriovenous malformations.
§Expected severe morbidity at 6 months according to expert panel.

between observed and expected outcomes. Table I summarises the data within the six diagnostic groups, and details for each diagnosis are included in the appendix. There was a wide variation in estimated costs (and confidence intervals) of averting a death or severe disability: for example, £41 per QALY for extradural haematoma, £25 039 for cerebral metastases, and £68 694 for malignant brain tumours.

COSTS OF AVERTING SEVERE DISABILITY ALONE

Data on expected outcome of subarachnoid haemorrhage are precise enough to allow separate analysis of death and severe disability (table II). The expert panel's opinion was used to assess outcome after head injury, chronic subdural haematoma, and cerebral abscess as examples of conditions that can lead to severe disabilities. Such an analysis assumes the cynical view that death is cheap, and a conservative estimate of the cost of long term care of £50 a day was used. Even with this unacceptable abstraction it remained cost effective to avert severe disability, the total cost of neurosurgical intervention in these four groups being £0·56 million compared with £10·33 million for long term care if they were untreated.

Discussion

Our study shows that in Britain neurosurgery is not expensive in comparison with the costs and benefits of other areas of medicine and, with the exception of a few specific conditions, the cost per QALY is unexpectedly low. This is the context in which a neurosurgical budget should be assessed.

Limitation of resources is causing those responsible for health care to look critically at the costs and benefits of services provided. Although it should be quite easy to define cost in financial terms, it is difficult to define and quantify effectiveness and benefit. There is a danger that the quest for cost effectiveness will suppress the traditional values of caring and humanity that have been characteristics of our health services, especially in the state funded sector. In this regard neurosurgery, a relatively small and seemingly expensive specialty, is suitable for critical cost-benefit analysis.

MEASUREMENT OF COSTS

The estimated figure for neurosurgical care included all ancillary investigations, portering, rates, etc, but not the capital cost of replacing the building. Winyard *et al* estimated average costs of a neurosurgical bed in Oxford, where provision is similar to Wessex, to be about £100 a day in 1980-1.[2] This value compares reasonably well with our estimate of £146 a day in 1984, allowing for 37% inflation in the intervening period. These costs are lower than at Kuopio University Central Hospital in Finland, where in 1988 the net cost per day was 1903 Finnish marks (about £270, see below).

It was not possible to calculate separate costs per day for each diagnostic group, nor the costs before and after the stay in the neurosurgical unit, for this would have entailed investigating nursing dependency, theatre use, diagnostic imaging, and other aspects of treatment and would have needed a prospective study. There is evidence, however, from diagnosis related reimbursements for Medicare quoted in the *United States Federal Register* (appendix, table A7) that using average bed day costs will not significantly distort the final results. Thus, although the American diagnostic groups are not the same as those used in our study, the relative costs per bed day of different types of neurosurgical care fall (with only one exception) within the narrow range of 0·21 to 0·24.

OUTCOME AND BENEFITS OF NEUROSURGICAL MANAGEMENT

Because information was derived from neurosurgical service records inclusion of eligible cases was reasonably complete. Only 10% of all cases and 6% of patients with available case notes were not followed up. This small proportion is unlikely to be a source of bias, but as hospital activity analyses were not available for the year of study we were unable to determine whether the cases not followed up were atypical.

The Glasgow outcome scale has been well validated.[9,10] We used it to take account of those patients who had not made a good recovery but who had neither died nor been left severely disabled. The results of more detailed assessments of quality of survival,[1,13,14,21,22] which can be used only prospectively, should fall within our range of costs per QALY. It has been shown[23] that there is reasonable agreement between patients' and doctors' evaluation of results after neurosurgery, provided preoperative counselling has been realistic.

The expected outcome without neurosurgical intervention varies from the well defined (for example, subarachnoid haemorrhage) to the reasonably obvious (for example, malignant brain tumours) and the less obvious. The possibility that the expert panel might have been too pessimistic has been examined by comparing its assessments with published studies and by reporting the range of panel members' opinions (appendix, tables A2-A6). The order of magnitude of the costs per QALY and the conclusions to be drawn are not affected by variations in the views of members of the expert panel for diagnostic groups with reasonable numbers of patients. Wide fluctuations are, however, seen in very small diagnostic groups with a broad spectrum of severity of presentation.

COMPARISON OF COSTS PER BAD OUTCOME AVERTED AND PER QALY

Information on the costs of saving a life is scant and rarely available on a comparable basis for a range of conditions. Roberts *et al* estimated the costs in 1981-2 of a number of conditions, and they ranged from as little as £100 per life saved to over £900 000[24] (tables III

and IV). Within this range neurosurgery seems to be good value for money, falling within the criteria used by Roberts *et al* in defining "affordability" within the NHS. Neurosurgical procedures on the spine are little more expensive, in terms of benefit, than hip replacement, and because they tend to be on younger patients they are considerably cheaper per QALY. The costs may also be compared with the estimates provided by Buxton *et al* for heart transplants, of £16 000 in the first year with a one year survival of 70%, the cost per death averted at one year therefore being about £23 000 assuming zero survival without operation[25]—between two and four times as expensive as most neurosurgical procedures.

COMPARISON OF NEUROSURGICAL COSTS INTERNATIONALLY

Our results allow comparison between units in the United Kingdom and those abroad. Kuopio University Central Hospital (M Vapalahti, personal communication) had a neurosurgical inpatient budget for 1988 of 19 million Finnish marks (£2·7 million), which included £360 000 for purchasing services from other hospitals (but not all the indirect costs which were included in Rees's report for Wessex).[8] In 1988, 1374 patients were admitted (*v* 1026 in Wessex in 1984) for a mean stay of 6·4 (*v* 12·5) days; 1000 major operations were performed at a cost of £2700 (*v* £2500) per patient. It would be useful to compare estimates of outcome and benefit achieved. In France, Cohadon has provided estimates of the cost of managing 14 patients with malignant glioma from diagnosis to death.[29] No estimate of the product of care was made, but one day of survival in such a patient cared for normally until death cost the community Fr 375 (£36). In Wessex the increased cost over the natural course of this condition was £900 per day, but this included patients being studied in multicentre trials who were kept in the neurosurgical department longer than they would otherwise have been, and who because of the trials also had additional brain scans both as inpatients and as outpatients.

Measurement of benefits in the way we have described should enable a start to be made in comparing different health systems, so that advantageous and disadvantageous aspects can be identified.

TABLE III—*Cost of avoiding one death or long term disability (1983-4 prices)*

General*	Cost (£)	Neurosurgery
Pre-operative chest *x* ray	1 000 000	
Cervical cancer screening	54 000–285 000	
Breast cancer screening	39 000–80 000	
	68 000	Malignant brain tumours
Open spina bifida	22 000	
Sudden infant death†	16 000	
Whole body scan	11 000	Metastatic tumours in central nervous system
Open heart surgery	10 000	
Kidney transplant	8 000	
	7 000	Subarachnoid haemorrhage
	5 500	Head injury; benign intracranial tumours
	5 000	Spinal disorders
Hip replacement	2 000	
Operation for perforated peptic ulcer	1 500	
Routine estimation of haemoglobin concentrations	200	
Blood pressure screening	100	

*Figures from Williams,[15] Roberts *et al*,[24] Buxton *et al*,[25] Charny *et al*,[26] Vermeer *et al*,[27] Knox.[28] Corrected for inflation to 1983-4 prices with retail price index where necessary.
†Surveillance by health visitor.

TABLE IV—*Cost per QALY (1983-4 prices)*

General*	Cost (£)	Neurosurgery†
	69 000	Malignant brain tumours
Haemodialysis in hospital	14 000	
Coronary artery bypass graft for moderate angina and one diseased vessel	12 000	
	11 000	Metastatic tumours in central nervous system
Heart transplantation	5 000	
Cervical cancer screening	2 500–15 000	
Breast cancer screening	3 000	
Renal transplantation	3 000	
Coronary artery bypass graft for disease in main vessels	1 040	
Thrombolytic treatment for acute myocardial infarction	600–3 000	
Hip replacement	750	
Inserting pacemaker for atrioventricular heart block	700	
	350	All neurosurgery
	310	Subarachnoid haemorrhage
	300	Miscellaneous
	260	Spinal disorders
	240	Benign intracranial tumours
	150	Head injury

*Figures from Williams[15]; Roberts *et al*[24]; Buxton *et al*[25]; Charny *et al*[26]; Vermeer *et al*[27]; Knox.[28] Corrected for inflation to 1983-4 prices with retail price index where necessary.
†Neurosurgical QALY refers to deaths and severe disabilities averted and has been modified to take account of proportion of patients left moderately disabled.

IMPLICATIONS FOR NEUROSURGICAL RESOURCES AND SELECTION OF PATIENTS

If cost effectiveness is to be used as a factor in selecting patients for neurosurgical care then society may have to accept attitudes that conflict with the more traditional humane approach. Examples of this conflict are the current poor cost-benefit of neurosurgical management of patients with malignant brain tumours compared with the favourable cost-benefit of surgery for epilepsy.[30] The selection of patients whose management is cost effective must be accompanied by a clear intent to improve management that is currently ineffective. Controlled trials are costly and difficult but can contribute greatly to future cost effectiveness, so that the cost of establishing competent research teams should be seen in the light of long term potential savings.

A good example of the financial advantages of initiating costly technical advances is available from spinal investigation. In the Mersey Regional Neuroscience Unit the total annual direct cost of myelography in 1986 was at least £486 000.[31] Replacing myelography with magnetic resonance imaging will improve patient comfort, safety, and diagnostic accuracy and is also financially appealing.[32] Another example is the use of the calcium antagonist nimodipine, which was shown in a large controlled trial to reduce bad outcome after subarachnoid haemorrhage.[33] Data in the appendix (table A1) show that there would be about 11 fewer bad outcomes a year to be set against the cost of nimodipine (about £43 000 a year) for an average neurosurgical unit. Hence each bad outcome averted by nimodipine costs about £3900, but each severe disability not averted costs at least £474 000 in long term care. It is essential to consider the apparent additional expense of a new drug such as nimodipine in the context of the overall cost effectiveness of patient management rather than simply in terms of the immediate burden on the neurosurgical budget (I Williams, personal communication).

BUDGETING AND SERVICE CONTRACTS

The true cost of neurosurgical services is difficult to estimate from existing information. Neurosurgeons bear responsibility for many patients whom they never see directly but whom they help to manage by telephone consultation and the creation of guidelines. A regional health authority spends a large but as yet unidentified sum on patients with neurosurgical conditions who are never admitted to the regional unit. Medical admissions to neurosurgical units also consume resources, and outpatient consultation forms a significant part of the workload. The extent to which all these activities contribute to the wellbeing of a population is at present impossible to quantify. More strenuous efforts should be made to assess the benefits of these activities, which could be jeopardised if funding was based solely on cost-benefit of neurosurgical procedures.

The changes in the relationships between hospitals

and health authorities under the new NHS contract make our results immediately relevant. When establishing contracts for services health authorities will want to look closely at the costs and benefits of what they buy and hospitals will have to consider in detail the relative costs, benefits, and effectiveness of what they provide. Any studies of cost-benefit must, however, take into account the overall case mix and the demands of training. If low cost but profitable conditions are "stripped off," leaving regional neurosurgical units with only the high cost, difficult problems,[34] the training of the next generation of neurosurgeons, neuropathologists, neuroradiologists, and neurosurgical nurses will suffer. Contracts will have to be based on a broad spectrum of patients reflecting conditions in a complete population.

Finally, purchasing authorities will continue to want access to the fruits of research that are currently made available. Efficient local and national mechanisms will have to be devised to share the costs of research and development among the purchasers and thus provide a secure basis for future developments and advances in a specialty that, despite its traditional reputation, is not an expensive surgical Cinderella.

Appendix

TABLE A1—*Probable cost of product of care for subarachnoid haemorrhage*

Diagnosis	No of patients (No not followed up)	Length of stay (days) Total	Mean	Total cost (£)	Bad outcomes Observed (at 6 months)	Expected (at 20 years)	Expected minus observed	Cost per bad outcome averted (£)	Mean age (% men)	Life expectancy (years)*	Cost per aLY (£)†	Cost per QALY (£)‡
Haemorrhage due to aneurysm, arteriovenous malformation, and spontaneous intracerebral haematoma	99 (7)	1540	15·6	224 840	19	61§	42	5353	43 (45)	31	173	192
Aneurysm (unruptured)	10	131	13·1	19 126		3‖	3	6375	50 (40)	25	255	300
Negative angiography or miscellaneous	69 (6)	566	8·2	82 636	8	8		∞	52 (32)	23	∞	∞
Total (mean)	178	2237		326 602			45	(7258)		(26)	(279)	(310)

*Corrected according to Hawkins *et al.*[12]
†Includes deaths and severe disabilities averted.
‡Corrected for proportion of patients who remained moderately disabled, assigning a value of 0·5 rather than 1 to the quality of such a life; the proportions with moderate disability and good recoveries were known for each diagnostic group.
§Based on known clinical grade and time from ictus on admission as documented by Shaw *et al*[36] and using the prognostic methods described by Pakarinen,[37] Graf,[38] Alvord *et al*,[39] Winn *et al*,[40] panel estimate 69 (range 59-78).
‖Estimate of expert panel.

TABLE A2—*Probable range of values for cost of product of care for head injury*

Diagnosis	No of patients (No not followed up)	Length of stay (days) Total	Mean	Total cost (£)	Bad outcomes Observed (at 6 months)	Expected (at 6 months)	Expected minus observed (95% CI*)	Cost per bad outcome averted (£) (95% CI)	Mean age (% men)	Life expectancy (years)	Cost per aLY (£)† (95% CI)	Cost per QALY (£)‡
Extradural haematoma	19 (1)	165	8·7	24 090	3	17	14 (12 to15)	1 721 (1 606 to 2 008)	28 (79)	46	37 (35 to 44)	41
Intradural haematoma (acute)	11	118	10·7	17 228	5	10	5 (4 to 6)	3 446 (2 871 to 4 307)	47 (50)	34	101 (84 to 127)	135
Diffuse and unspecified§	86 (13)	589	6·8	85 994	18	18	0 (−3 to 4)	∞ (21 499 to ∞)	32 (83)	42	∞ (512 to ∞)	∞
Compound depressed fracture‖	26 (1)	164	6·3	23 944	2	6	4 (−1 to 11)	5 986 (2 177 to ∞)	25 (69)	50	120 (44 to ∞)	125
With cerebrospinal fluid, rhinorrhoea, or otorrhoea¶	3	47	15·7	6 862		1	1 (0 to 1)	6 862 (6 862 to ∞)	26 (100)	47	146 (146 to ∞)	146
Chronic subdural haematoma**	16	234	14·6	34 164	2	13	11 (5 to 14)	3 106 (2 440 to 6 833)	70 (63)	11	282 (222 to 621)	303
Total (mean)	161	1317		192 282			35	(5 494)		(40)	(137 (37 to ∞))	(151)

*Of range of opinion of expert panel.
†Includes deaths and severe disabilities averted.
‡Corrected for proportion of patients who remained moderately disabled, assigning a value of 0·5 rather than 1 to the quality of such a life; the proportions with moderate disability and good recoveries were known for each diagnostic group.
§Of 34 severe (coma > 6 hours) five were not followed up, leaving 29 for analysis; 11 had "avoidable factors."
‖For discussion of prognostic factors, see Jennett and Teasdale[10] and van den Heever and van der Merwe.[41]
¶Persistent; for discussion of prognostic factors see Jennett and Teasdale.[10]
**Failed conservative management—all operated on; see Bender and Christoff,[41] Gjerris and Schmidt,[42] Bartlett[43] for discussion of conservative management with average duration of treatment of six weeks.

TABLE A3—*Probable range of values for cost of product of care for intracranial tumours*

Diagnosis	No of patients (No not followed up)	Length of stay (days) Total	Mean	Total cost (£)	Bad outcomes Observed (at 6 months)	Expected (at 20 years)	Expected minus observed (95% CI*)	Cost per bad outcome averted (£) (95% CI)	Mean age (% men)	Life expectancy (years)	Cost per aLY (£) (95% CI*)†	Cost per QALY (£)‡
Malignant:												
Glioma plus miscellaneous	108 (17)	1 751	16·2	225 646	65	66§	1 (−7 to 10)	255 646 (25 565 to ∞)	51 (61)	0·77y‖	332 008 (33 201 to ∞)	400 010
Ependymoma	7 (1)	98	14	14 308	3	5¶	2 (2 to 3)	7 154 (4 769 to 7 154)	29 (29)	6**	1 192 (795 to 1 192)	1 419
Medulloblastoma	1	27	27	3 492		1¶	1	3 942	18	4**	788	788
All malignant tumours (mean values)	116	1 876		273 896			4	(68 474)		(1·12)	(61 138)	(68 694)
Benign:												
Pituitary	37 (2)	543	14·7	79 278	1	23¶	21 (14 to 28)††	3 775 (2 831 to 5 663)	48 (68)	28	135 (101 to 202)	148
Meningioma	28	632	22·6	92 272	6	20¶	11 (7 to 16)‡‡	8 388 (5 767 to 13 182)	52 (39)	27	312 (214 to 490)	351
Acoustic	8	169	21·1	24 674	1	6¶	5 (3 to 6)§§	4 935 (4 112 to 8 225)	55 (25)	24	206 (171 to 343)	317
Craniopharyngioma	4	64	16·0	9 344	2	3¶	0·5 (0 to 0·5)‖‖	18 688 (18 688 to ∞)	26 (25)	51	366 (366 to ∞)	366
Haemangioblastoma	5 (1)	81	16·2	11 826	1	3¶	1·5 (1·5 to 2)¶¶	7 884 (5 913 to 7 884)	58 (60)	20	394 (296 to 394)	588
All benign tumours (mean values)	82	1 489		217 394			39	(5 574)		(28)	(199)	(243)

*Of range of opinion of expert panel.
†Includes deaths and severe disabilities averted.
‡Corrected for proportion of patients who remained moderately disabled, assigning a value of 0·5 rather than 1 to the quality of such a life; the proportions with moderate disability and good recoveries were known for each diagnostic group.
§Expected outcome at 6 months.
‖80% High grade malignancy; 20% low grade malignancy.[12 45 47]
¶ Expected outcome after 20 years(opinion of expert panel).
**Bloom.[44]
††Allows for late recurrence of symptoms in 5% of patients after radiotherapy.[46]
‡‡Corrected for late recurrence of 19%; Simpson[50]; Mirimanoff *et al*[51]; Weeks.[52]
§§Allows for late recurrence of 10%.
‖‖Corrected for late recurrence of 50%.[46 47]
¶¶Corrected for late recurrence, second tumour, or systemic complications of von Hippel-Lindau in 25% of patients.

TABLE A4—*Probable range of values for cost of product of care for non-metastatic spinal disorders*

Diagnosis	No of patients (No not followed up)	Length of stay (days)		Total cost (£)	Bad outcomes		Expected minus observed (95% CI*)	Cost per bad outcome averted (£) (95% CI)	Mean age (% men)	Life expectancy (years)	Cost per aLY (£) (95% CI*)†	Cost per QALY (£)‡
		Total	Mean		Observed (at 6 months)	Expected (at 6 months)						
Congenital§	11 (1)	98	8·9	14 308		4	4	3 577	13 (45)	63	57	76
Lumbar prolapsed intervertebral disc‖	43 (1)	648	15·1	94 608	4	22	18 (12 to 26)	5 256 (3 639 to 7 884)	42 (35)	35	150 (104 to 225)¶	183
Lumbar spondylosis‖	41 (4)	547	13·3	79 862	7	22	15 (9 to 21)	5 324 (3 803 to 8 874)	57 (59)	21	254 (181 to 423)¶	339
Cervical spondylosis‖	37 (3)	538	14·5	78 548	5	18	13 (10 to 17)	6 042 (4 620 to 7 855)	58 (69)	20	302 (231 to 393)¶	451
Extramedullary tumours and angioma**	13	187	14·4	27 302	4	12	8 (6 to 9)††	3 413 (3 034 to 4 550)	59 (31)	21	163 (144 to 217)	226
Intramedullary tumours‡‡	14 (4)	268	19·1	39 128	3	9	6	6 521	45	19§§	343	476
Total (mean)	159	2 286		333 756			64	(5 215)		(27)	(193 (57 to 343))	(261 (76 to 476))

*Of range of opinion of expert panel.
†Includes deaths and severe disabilities averted.
‡Corrected for proportion of patients who remained moderately disabled, assigning a value of 0·5 rather than 1 to the quality of such a life; the proportions with moderate disability and good recoveries were known for each diagnostic group.
§Four operations.
‖Failed conservative management; expected outcome based on number of patients operated on: lumbar prolapsed intervertebral disc 34; lumbar spondylosis 31; cervical spondylosis 23.
¶Cost per life year based on 20 year expected outcome: lumbar prolapsed intervertebral disc £169; lumbar spondylosis £211; cervical spondylosis £262.
**Neurofibroma, schwannoma, meningioma, angioma.
††Allows for up to 5% late recurrence.
‡‡Astrocytoma, ependymoma, miscellaneous; nine operations.
§§Crude estimate: approximately 15% complete excision (Northfield[4]); life expectancy ranges from 23·5 for incomplete paraplegia to 12 for complete tetraplegia (Geisler *et al*[14]).

TABLE A5—*Probable range of values for cost of product of care for central nervous system metastases*

Diagnosis	No of patients (No not followed up)	Length of stay (days)		Total cost (£)	Bad outcomes		Expected minus observed (95% CI*)	Cost per bad outcome averted (£) (95% CI)	Mean age (% men)	Life expectancy (years)†	Cost per aLY (£) (95% CI*)†
		Total	Mean		Observed (at 6 months)	Expected (at 6 months)					
Cerebral metastases‡	29 (2)	343	11·8	50 078	21	23	2 (0 to 4)	25 039 (12 520 to ∞)	56 (52)	1	25 039 (12 520 to ∞)
Spinal metastases§	37 (12)	267	7·2	38 982	18	22	6 (3 to 9)‖	6 497 (4 331 to 12 894)	64 (61)	1	6 497 (4 331 to 12 994)
Total (mean)	66	610		89 060			8	(11 133)			(11 133)

*Of range of opinion of expert panel.
†Determined from notes and telephone follow up.
‡Lymphoma 2; lung, kidney, breast, melanoma, colon, unknown.
§Lymphoma/myeloma 3; lung, breast, prostate, bowel, bladder, stomach, leiomyosarcoma, sarcoma, unknown.
‖ Corrected in proportion for number of patients not followed up.

TABLE A6—*Probable range of values for cost of product of care for miscellaneous conditions*

Diagnosis	No of patients (No not followed up)	Length of stay (days)		Total cost (£)	Bad outcomes		Expected minus observed (95% CI*)	Cost per bad outcome averted (£) (95% CI)	Mean age (% men)	Life expectancy (years)	Cost per aLY (£) (95% CI*)†	Cost per QALY (£)‡
		Total	Mean		Observed (at 6 months)	Expected (at 6 months)						
Abscess	12	267	22·3	38 982	4	11	7 (6 to 8)	5 569 (4 873 to 6 497)	45 (55)	31	180 (157 to 210)	222
Hydrocephalus	45 (2)	609	13·5	88 914	14	29	16 (9 to 22)§	5 557 (4 042 to 9 879)	43 (58)	33	168 (122 to 299)	215
Trigeminal neuralgia	12 (1)	109	9·1	15 914		9‖	9	1 768	61 (25)	16	111	128
Encephalitis or meningitis	13 (1)	117	9·0	17 082	1	8	7 (4 to 9)	2 440 (1 898 to 4 271)	40 (54)	36	68 (53 to 119)	76
Benign intracranial hypertension¶	7 (2)	134	19·1	19 564		1	1 (1 to 2)	19 564 (9 782 to 19 564)	38	41	477 (239 to 477)	681
Carpal tunnel syndrome**	4	22	5·5	3 212		4	4	803	55 (25)	24	34	34
Epilepsy	10 (6)	53	5·3	7 738	2	3‡‡	1	7 738	40 (40)	37	209	279
Cerebrovascular (non-haemorrhagic)	50 (25)	395	7·9	57 670	8	10‡‡	2	28 835	53 (50)	25	1 153	1 558
Unclassified or miscellaneous	63 (24)	670	10·6	97 820	23	24‖‖	1	97 820	44	30	3 260	4 180
Total (mean range)	216	2376		34 896			48	(7 227)		(30)	(241 (34 to 3 260))	(307)

*Of range of opinion of expert panel.
†Includes deaths and severe disabilities averted.
‡Corrected for proportion of patients who remained moderately disabled, assigning a value of 0·5 rather than 1 to the quality of such a life; the proportions with moderate disability and good recoveries were known for each diagnostic group.
§Corrected for number of patients not followed up.
‖ Nine operations; Sharr.[33]
¶Three operations.
**Four operations.
††Two severely disabled before treatment; one status epilepticus.
‡‡Two operations for cerebellar infarction.
‖‖ One operation for cervical rib.

TABLE A7—*Reimbursements for Medicare related to diagnosis (from United States Federal Register[20])*

Diagnosis related group		Relative weight	Relative weight per bed day
001	Craniotomy except for trauma (age >17)	3·49	0·24
002	Craniotomy for trauma (age >17)	4·14	0·31
003	Craniotomy (age 0-17)	2·92	0·23
004	Spinal procedures	2·68	0·21
005	Extracranial vascular procedures	1·56	0·24
006	Carpal tunnel release	0·45	0·22
007	Peripheral and cranial nerve and other nervous system procedures with complications and comorbidity	2·83	0·24
008	Peripheral and cranial nerve and other nervous system procedures without complications and comorbidity	0·74	0·22

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Sodium-lithium countertransport activity in red cells of patients with insulin dependent diabetes and nephropathy and their parents

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Abstract

***Objective*—To determine whether there are familial and genetic aspects of sodium-lithium countertransport activity in red cells in diabetic nephropathy.**

***Design*—Case-control study.**

***Setting*—Teaching hospital diabetic clinic.**

***Subjects*—40 Patients with insulin dependent diabetes, both of whose parents were alive: 20 with persistent proteinuria and 20 with normal albumin excretion matched for age, duration of diabetes, and body mass index. All 80 parents.**

***Main outcome measures*—Sodium-lithium countertransport activity in red cells and arterial blood pressure.**

***Results*—Sodium-lithium countertransport activity in red cells was higher in the patients with proteinuria than in the patients with normoalbuminuria (mean (95% confidence interval) 0·47 (0·39 to 0·54) *v* 0·33 (0·28 to 0·38) mmol/l red cells/h respectively, p=0·0036; mean difference 0·14 (0·04 to 0·22)). The mean countertransport activity for the two parents of each patient was calculated, and from this the mean value for each group of parents was calculated; the value was higher in the parents of the patients with proteinuria than in the parents of the patients with normoalbuminuria (0·40 (0·32 to 0·48) *v* 0·30 (0·26 to 0·33) mmol/l red cells/h respectively, p=0·016; 0·10 (0·02 to 0·19)). Twenty eight of the parents of the patients with proteinuria compared with 12 of the parents of the patients with normoalbuminuria had a countertransport activity that was above the median value in all 80 parents (p<0·001). Mean arterial blood pressure in the parents of the patients with proteinuria was related to that of their offspring (r=0·46; p<0·01). There was a positive correlation between the sodium-lithium countertransport activity in red cells in the parents and their offspring when all parents and patients were considered (r=0·37; p<0·001).**

***Conclusions*—Increased sodium-lithium countertransport activity in red cells in the parents of diabetic patients with nephropathy provides further evidence that familial, and possibly genetic, factors related to a predisposition to arterial hypertension have a role in the susceptibility of diabetic renal disease.**

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Introduction

The factors that predispose a substantial subset of diabetic patients to the serious complication of diabetic nephropathy have not been elucidated.[1] Although poor glycaemic control may play some part, it is unlikely to be the sole determinant.[2-5] Recent work has shown that diabetic nephropathy clusters in families, the frequency of nephropathy in diabetic siblings of diabetic probands with nephropathy being five times that in diabetic siblings of diabetic probands without nephropathy.[6] The importance of familial factors, and thus possibly heredity, has been further emphasised